
EUROPA UOMO 

The Voice of Men with Prostate Cancer In Europe

**Annual Report
of the Board
for 2018/19**



Above: Photo by Erik Briers of the **Delegates in Malahide GA2018**

Below: **Patient Empowerment**



1. Chairman's Note

The last year has passed incredibly quickly. It is already a year since I was elected as chairman of Europa Uomo during the General Assembly in Dublin.

Together with the Board and our members, we have worked hard to grow further the organisation and fulfil our mission of being the voice of men with prostate cancer in Europe.

We have increased our communication efforts through our newsletter and our website. It is possible to read our website in many languages and our newsletter attracts more and more readers. But there is still a lot of work to do.



Together with all our members we undertook a survey and the results show that the knowledge of prostate cancer in most European states is no higher than 50% and there is a big inequality in cancer care.

Here are some figures:

- Less than 50% of all men are aware of the disease
- PSA-led early detection is promoted by healthcare professionals in only 50% of the countries
- Depending on the country, between 20 and 60% of all PCa diagnosis is done in the metastatic phase
- A multidisciplinary approach is partially available, not all treatments are available in all countries. Inequality of care is the norm

There is also good news. The EAU has finally decided on major change following the long-running debate on PSA-led screening for prostate cancer. In the new guidelines (2019) screening is now recommended as the new standard. The last year's data has shown that, providing the screening is done in accordance with the new EAU guidelines, the results of screening (in terms of lives saved) are as good, if not better, than screening for colon or breast cancer. This is without even taking into account the benefits, in terms of the quality of life of prostate cancer patients, that early diagnosis brings.

Unfortunately, men cannot influence whether, they develop PCa, nor whether it will be a slowly developing low risk, or a highly aggressive cancer. What men (and policy makers) can influence is an early detection of this cancer.

If you are diagnosed at an early stage, your quality of life is affected, but to a much lesser extent than detection in a metastatic phase. This is specially true when treatment is carried out in a cancer centre with experienced surgeons,

radiotherapists and medical oncologists. Detection in advanced or metastatic phase means a lifetime of hormone treatment which often has the following side effects: impotence, fatigue, osteoporosis, loss of libido and in a later treatment phase, chemotherapy.

In order to ensure that men receive the best possible treatment, and that over treatment is no longer an issue, when screening is adopted, we as patients must urge our politicians and policy makers to adopt a change in strategy based on three pillars. All three must be implemented at the same time to ensure the best treatment, with quality of life, and reduced overall cost. These pillars are:

- Increase awareness of the disease
- Promote informed PSA-led early detection
- Ensure treatment of PCa in multidisciplinary cancer centres

Increase awareness

It will be necessary to launch awareness campaigns as was done for breast and colon cancers. Men and their relatives need to be made aware that PCa exists and that curative treatment is possible, especially when detected at an early stage.

Promote informed PSA led early detection

It is important that informed men are actively encouraged by their government and healthcare professionals to test their PSA level. The scientifically based advice on when to test is described in the newly published EAU guidelines. They insist on an individual early diagnosis in informed healthy men with a life expectancy of 10 to 15 years. If there is a suspicion of PCa based on the PSA test a mpMRI scan should be performed before deciding on a biopsy. Diagnosis starts at 45 to 50 years depending on risk analysis and family history. Depending on life expectancy, 70 years should not always be the end date of PSA-led early detection.

Ensure treatment in multidisciplinary cancer centres

Considering the best outcome for men, treatment in a cancer centre with a multidisciplinary approach is a must. Studies have shown that the extent and severity of the side effects of treatments are a function of the experience of the surgeon and/or radiotherapist.

We expect cancer centres to measure the patient-related outcomes and have them published and freely accessible for patients.

Different initiatives have been taken to establish prostate cancer centres. Germany for instance, has developed its own requirements. From a patient point of view, as long as the general idea is maintained and all treatments are ensured, we can live with these developments.

The development of active surveillance treatment for men with low-risk PCa is essential in order to avoid over-treatment and to ensure an optimal quality of life for the patient for as long as he can stay in that programme. It is also important to realise that active surveillance is a treatment in itself, and, should be considered as valid as any other treatment in Stage I and Stage II of the disease. Active surveillance should not be confused with the watchful waiting programmes in the later stages of the cancer.

In the last three years, a lot of progress has been made and knowledge gathered on how to apply active surveillance safely. Generally, there is a belief that this treatment can be valid for up to 30% of patients – those with low or intermediate risk.

It is up to Europa Uomo and its members to insist that screening is implemented as described above.

As you will read in this report, our projects are still the driver of our actions. You will discover that we have rearranged and adapted some projects and added some new ones. This is a result of our experience in working with projects over the last three years and a sign of our continuous improvement. We also try to link expenditure as much as possible to our projects. As such, we continue to improve our efficiency and assign our limited resources (money and human resources) where they are likely to have the most effect.

I would like to say thanks to all who have contributed to our efforts this year. Not in any specific order: our members, volunteers, our secretariat, sponsors, scientific advisors, healthcare professionals, Board members, LOCs and all those members of committees and meetings who have listened to our concerns and have allowed us to share our views.

Finally, a special thanks to Tackle UK for hosting our general assembly this year.

André Deschamps
Chairman

2. Executive Summary

- ❖ **Board Meetings:** The Board met seven times since the last General Assembly. These meetings are listed below at section 3.
A further meeting will take place on the morning of the GA in Birmingham.

- ❖ **Strategy:** The Board sought to implement the Strategy adopted by the GA in 2015/16 and as modified by the GA in 2017. Key steps have been taken to realise the development of the organisation in eastern Europe and in the implementation of a training programme. See separate GA agenda proposals to admit new members and the WECAN training programmes.

- ❖ **EPAD:** The Board staged a joint event with the EAU for European Prostate Awareness Day which marked a turning point in the approach of both the medical profession and the patient organisation regarding prostate cancer screening as an aid to early detection and the avoidance of over-treatment. The EPAD was held on 22 January in the European Parliament in Brussels. See more a detailed report below at Section 4, Goal 1 and also the EAU Policy Paper on Prostate Cancer Screening at Appendix 3.

- ❖ **Meetings:** Board members attended a number of conferences and meetings. A listing of all meetings attended are set out in Appendix 4 and where available short reports of the main events are provided in the Update newsletter and on the website. See also Section 7 of this Report.

- ❖ **European Medicines Agency:** The EMA has moved from London to Amsterdam as a consequence of the UK's referendum decision to leave the EU. Europa Uomo members continue to participate in its regulatory work. The Board has sought renewal of its membership of Working Parties and continues to nominate representatives to scientific committees, working parties and advisory groups in relation to medicines applications and usage. See the report of Erik Briers on CAT in Appendix 5.

- ❖ **Membership:** Less than a year after it joined Europa Uomo our Estonian affiliate suffered the loss of its President. This was a difficult period for the organisation, but with the support of Board member Pentti Tuohimaa, the Estonian organisation resumed activity again, but this time the lightning did strike again in that their new leader Niilo Saard became another victim to our disease, so

matters are again in flux. See below and Vice Chairman's report in Appendix 1. Notwithstanding these setbacks in Estonia the Board is pleased to be able to put four applications for membership before the GA.

The Board has renewed its arrangement with Gladiator which enables the continued employment of Izabella Pawlowska. See Section 4, Goal 4.

- ❖ **Organisation: Liaison Officers:** The role of Liaison Officers was reviewed during the year. The Board will consult with the LOCs and the membership before further developing the role during the coming year. In the meantime, the GA has been asked to amend the Bye-Laws so that the same term limits apply to LOCs as Board members. See Section 4, Goal 5.
- ❖ **Communications:** The Board continues to strive to develop its communications strategy. The Board has accepted further proposals from communications consultant Simon Crompton, seeking to make the strategy more focussed and effective. See Section 4, Goal 5.
- ❖ **Funding and Financial Report:** In keeping with the changes last year in presentation of the financial report, the Board has continued to recast expenditure to support the shift to project-based activity. The report also includes the audited Balance Sheet for 2018 and the projected Outturn 2019 and an Outline Budget for 2020. See Section 5.
- ❖ **Meetings:** Attendance at meetings is a necessary, if unglamorous, part of the representation of men with prostate cancer. Our principal activities on this front are set out in Section 6 and a full listing is given in Appendix 4.

APPENDICES

- Appendix 1** Membership Development – Stig Lindahl
- Appendix 2** WECAN Training Programme
- Appendix 3** EAU Policy Paper on Prostate Cancer
- Appendix 4** Meetings and Conferences attended by Europa Uomo Board, Liaison Officers and representatives
- Appendix 5** EMA Scientific Committee on Advanced Therapies – Erik Briers

3. Board Membership

The Board has seven members each elected by the General Assembly for a term of three years, renewable for a further term of three years. At the GA in 2018, Chairman, Ken Mastris (UK), completed the second term of his membership of the Board and therefore stepped



An inflated prostate exhibit at GA 2018 Courtesy Janssen

down. Christian Arnold (France) also stepped down early from the Board for personal reasons. André Deschamps (Belgium) and John Dowling (Ireland) had completed their first term, but, were re-elected. The newly elected members were Guenther Carl (Germany) and Ioannis Vanezos (Cyprus).

The new Board met briefly before the end of the General Assembly at which the officers were elected. The full Board for 2018-19 was:

Chairman:	André Deschamps (Belgium)
Vice-Chairmen:	Will Jansen (The Netherlands) Stig Lindahl (Sweden)
Treasurer:	Ioannis Vanezos (Cyprus)
Secretary:	John Dowling (Ireland)
Other members:	Pentti Tuohimaa (Finland) Guenther Carl (Germany)

Ex-officio members nominated by partners:

Prof. Hein Van Poppel (EAU)
Dr. Alberto Costa (ESO)
Prof. Louis Denis (OCA)

The Board met seven times since the last General Assembly:

- 1) 05.07.2018 in Amsterdam
- 2) 13.09.2018 in Milan
- 3) 14.11.2018 in Brussels
- 4) 21.01.2019 in Brussels
- 5) 15.03.2019 in Barcelona
- 6) 29.04.2019 in Antwerp
- 7) 08.05.2019 Video Conference

An additional meeting will take place on 14 June before the GA.

In addition to the responsibilities set out in our Statutes for Chairman, Treasurer and Secretary, it is now customary for other Board members to take on particular portfolios.

Stig Lindahl with Pentti Tuohimaa have been developing our relations with patient organisations in eastern European and elsewhere and are pleased to bring four new candidate members for approval by the GA.

The responsibility for enacting the decision of the last GA to have a Quality of Life Survey was taken on by Guenther Carl. An account of the QoL survey is included in the projects report below.

Chairman André Deschamps continued to focus on the implementation of the organisation's strategy, developing our contacts with other patient organisations, and our sponsors and partners.

Our Secretary, John Dowling continued to deliver on the editorial role for the weekly *Update* and in the context of the WECAN initiative to develop suitable training opportunities for our members.

The Board is very grateful to our *ex-officio* members, nominated by our three partner organisations, for their assistance and advice during the year. Prof. Louis Denis has not been able to attend all of our Board meetings due to health restrictions on his travels. Prof. Hein Van Poppel has attended several Board meetings during the year and has been always available for valuable advice on a range of matters. Dr. Alberto Costa has not been able to attend the Board in person, but has been represented by deputies at a number of meetings.

This year two Board positions become vacant, where the incumbents have reached the end of their 3-year term. In one case, the member concerned, Vice-Chairman, Stig Lindahl, is stepping down, the other Vice-Chairman, Will Jansen, is standing again.

The election of Board members is undertaken by the Voting Delegates at the General Assembly.

The Board would like to pay tribute to the work of Liaison Officers, three of whom, Paul Enders, Maria Louisa Domingos and Joaquim Cruz Domingos have stepped down. Roger Wotton, Brigitte Dourcy-Belle-Rose, and Erik Briers continue in the role.

4. Europa Uomo Strategy – Goals



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The Strategy was adopted by the General Assembly in June 2016 and amended subsequently. The Board has continued to deliver on this strategy by means of various projects. The past and present Treasurers have incrementally recast the budgeting and disbursement of funds in accordance with this approach.

The Board has found that this policy has been welcomed by our sponsors and has greatly assisted the Board in obtaining new and additional sponsorship. From a management standpoint the Board, is able to control expenditure and to ensure that project delivery is monitored, in a timely manner.

Goal 1: Early Detection

- A major shift has occurred among urologists represented by the EAU in the course of the year. The EAU's prostate cancer guidelines have been amended to suggest that men should be fully informed by their physician before even undertaking a PSA blood test and that should the result be suspicious there should be no biopsy samples taken without a positive mpMRI. These steps, allied with EAU's extension of its practitioner education, are likely to result in a major reduction in overtreatment. In respect of low and very low risk patients the proportion who are offered and accept active surveillance (AS) has risen to two-thirds in the U.S. and in Europe the AS levels are well above that and in some countries like Sweden the AS rate is heading for 90% for the low and very low risk patients.
- Access to PSA testing is discouraged in some EU countries with the public authorities refusing to reimburse PSA testing and, by lack of information about prostate cancer risks and the effectiveness of early detection and treatment.
- The short-sighted approach of some public authorities is a good example of the English saying "*penny wise but pound foolish*". Prof. Hein Van Poppel has been in the vanguard in challenging this short-sighted approach. He has shown that delayed detection and treatment costs of metastatic prostate cancer is a

huge multiple of organized screening and treatment costs whereas higher risk disease can be identified early and treated effectively AND in a much more economic manner.

- The Board has sought to ensure that Europa Uomo and its member organisations are at the forefront of this campaign to have effective programmes of early detection. A joint meeting of EAU and EUomo under the EPAD banner was held in the European Parliament on 22 January and EUomo participation in a number of multilateral meetings since have sought to promote this approach. A slightly abridged version of the EAU's Policy Paper on prostate cancer screening is attached as Appendix 3 of this report.

Goal 2: Help establish Prostate Cancer Centers and raise quality to best international level in all European States

We reported in last year that:

- International Consortium of Health Outcome Measurement (ICHOM): Patient-Related Outcomes (PROs) for localized low/medium risk prostate cancer agreed and published.
- ICHOM PROs added to prostate cancer treatment guidelines and reports of certified prostate cancer centers, Germany.
- PROs for advanced prostate cancer agreed and published; Prof. Denis co-authored the ICHOM dataset for advanced prostate cancer.
- EAU will take the lead in establishing a limited number of expert PCUs in different countries.

In some EU states, prostate cancer centers are already in existence and Europa Uomo recognises that there will be different structures according to the legal and administrative provision in each country, but as long as the essential criteria for such centres are met, progress will be made. Europa Uomo (with the financial support of ESO) undertook its first audit of a PCU from a patient point-of-view at the Champalimaud Cancer Centre in Lisbon, Portugal. The next PCU patient audit is planned for July 2019 in the Rotterdam Hospital Group, in The Netherlands.

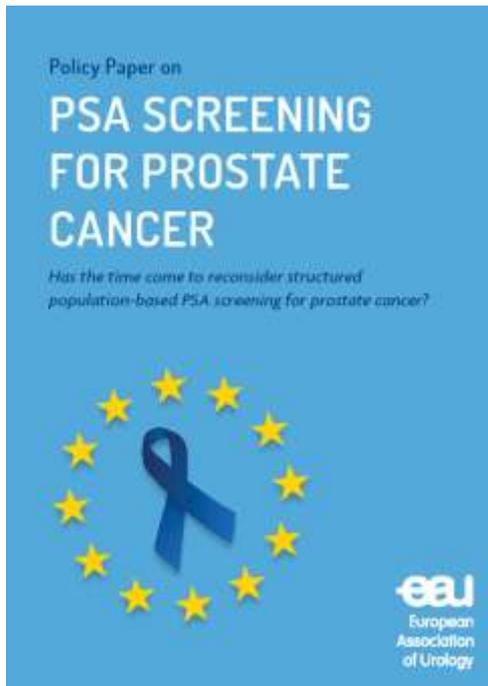
Goal 3: Therapy guidelines and patient information in all European States based upon best evidence

This goal includes three elements:

1. Europa Uomo representation in the EAU guidelines working group
2. To have in place up-to-date medical, scientific guidelines and patient guidelines in all European states.

3. Evidence of the application of those guidelines

- EAU guidelines (in 14 languages) and patient information sheets have been developed and are available.
- A patient representative, Erik Briers, is a member of the EAU prostate guidelines committee.



Those prostate guidelines are used as an input for guidelines in individual countries. For a variety of reasons, the country-specific guidelines are not always identical to the EAU guidelines.

The EAU's 'Patient Office' was established last year. Europa Uomo has been represented in the steering group which had led to the establishment of EAU Patient Advocacy Group (EPAG) with representative from a wide range of patient cancer organisations representing people with various genito-urinary cancers. The inaugural meeting of EPAG took place in Barcelona during the EAU19 Congress. John

Dowling and Guenter Carl are on the EPAG. Our former Chairman, Ken Mastris is representing ECPC on the EPAG.

The EAU operates a range of guidelines committees, of which the prostate cancer guidelines committee is one. The Europa Uomo representative is Erik Briers. The EAU Guidelines are reviewed continually and regularly updated such as the major changes year regarding the use of PSA screening and no biopsy without a positive MRI.

In 2017 there was a significant development of professional education in prostate cancer by the EAU. This was launched as PCa17 in Vienna in September of that year, Ken Mastris, Ekke Buchler, Erik Briers and John Dowling made up the patient cohort. The initiative was so successful that a further meeting, PCa18, was held in Milan, this time the patient cohort was swollen with the attendance of the full Board and a number of the LOCs. This had the same format, with two days of intensive workshops and plenary sessions attended by several hundred PCa specialists. A Board also held a meeting during the conference in Milan. The next such meeting -PCa19 - will be held in Prague later this year.

Goal 4: Encourage new support groups in European States

There is a gap in the provision of support for prostate patients between the “richer States” and “poorer States”. Europa Uomo encourages and supports patient groups in any and all European States, within and without the European Union. For some time it was a question of how could we turn this aim into a concrete reality. Contacts were established with cancer patient organisations and with the medical profession and successful efforts were made to develop several patient groups such as in Estonia with the tireless inputs from Pentti Tuohimaa and more recently in Armenia following a visit by Stig Lindahl and Latvia, following work by Izabella Pawlowska, backed up by Stig. Our member organisation in Bulgaria had become moribund and we had lost contact in recent years, but we managed to develop new contacts with the Bulgarian Association for Patient Defense (BAPD) which has now sought to affiliate to Europa Uomo. These developments arose from the organisational commitment and work over the past two years

We are very pleased to report that our arrangements with Gladiator, which has facilitated our employment of Izabella Pawlowska as Prostate Cancer Patient Officer, has been renewed. Some of the results of these efforts have been evident in the applications before the General Assembly this year from Armenia, Bulgaria and Latvia. An unexpected approach, following some contacts on active surveillance with some of our Irish colleagues in MAC and Stig Lindahl have developed into an application from the Icelandic patient organisation, Framför (Progress), to also join Europa Uomo. As we go to press an application has also been received from the Belgian organisation *Think Blue*.

This development process has required persistent hard work, but it eventually came to fruition and has encouraged to Board to look further afield to develop our organisation. The Board appreciates the financial support from our sponsors who have provided funding for this development work as well as the professional support from the medical organisations in Armenia, Poland, Latvia and Bulgaria. We also greatly appreciate the assistance and support of local cancer groups who have provided great assistance in bring some of these matters to a successful conclusion.

The work of Stig Lindahl, Pentti Tuohimaa, together with Izabella Pawlowska has been bearing fruit as evidenced by the new applications for membership of Europa Uomo and the better contacts with patient groups such as Europa Donna and national cancer organisations in many eastern European countries. It is hoped that these develop further in the coming year.

Goal 5: Develop Europa Uomo organisations, staff and funding

- The arrangement with our member organisation in Poland – Gladiator- has been continued and Izabella Pawlowska has agreed to continue in her role Prostate Cancer Patient Officer.
- The role of Liaison Officers was reviewed following the resignation of three LOCs. The Board has accepted that the role of the LOCs needs to be refined in the light of experience and before it appoints new Liaison Officers that it should ask the General Assembly to amend the Bye-Laws to introduce term limits on the appointment of new LOCs and apply them on a phased basis to existing LOCs. If this is agreed by the General Assembly the Board will seek to appoint a number of new LOCs from member organisations not currently represented at the Board and in consultation with the LOCs, to develop the role in a meaningful way to aid the work of the organisation.
- In accordance with Belgian Law and our Statutes and Bye-Laws, the changes in Board membership and the change in the location of the Secretariat were notified to the Belgian authorities and the provision in our statutes stating the address of the organisation's offices will need to be changed by amendment of the Statute Article 2, in due course.
- The Secretariat, maintained by Anja Vancauwenbergh, had to vacate the premises occupied since our organisation's inception due to the sale of the building by the Antwerp local authority. These premises were shared with the OCA (formerly the Oncology Centre of Antwerp and now the Ontmoetings Centrum Antwerpen (OCA) - the Meeting Centre Antwerp. Arrangements with the OCA for the use of the new premises, including financial terms, have been renewed and the occupation of the new offices took place towards the end of November 2018.

An EPAD (European Prostate Cancer Awareness Day) event was held at the European Parliament on 22 January 2019. The meeting was co-chaired by members of MAC (MEPs Against Cancer) with more than a dozen speakers, including our Chairman, André Deschamps. The meeting represented a major shift in the policy of the EAU on screening and it focused on the need for an effective screening programme, with early detection and treatment, including active surveillance. The meeting was attended by EAU representatives, Europa Uomo, MEPs and various clinical specialists.

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- The organisation's website www.europa-uomo.org has been further developed during the past year with the assistance of Simon Crompton, who many will have met as one of the facilitators at the pilot training programme last year. The main focus so far has been the editorial content and appearance of the Home Page together with social media platforms Facebook and Twitter. These changes have improved the number of visits to the site. John Dowling and Simon have been working to co-ordinate the weekly *Update* newsletter with the website and at the time of writing the Board has approved proposals for a greater degree of integration of the website and *Update* as well further developments.
 - *Update* - an email-based (MailChimp) newsletter was launched in February 2018 and by the time this Annual Report is considered at the GA it will have seen its 90th edition. The *Update* is sent to each member organisation and has been building slowly a readership outside the member associations. The *Update* seeks to provide the most recent information on prostate cancer research, any Europa Uomo news and items relating to cancer and prostate issues, genomics et cetera, which may be of interest to readers. All the medical material is lightened with a little levity – prostate cancer does not eliminate our sense of humour!
 - Development of patient training which was piloted at the GA last year, will be developed further within the WECAN training project which commences this July in Frankfurt. The Board has nominated two candidates each for the Smart Start Course and the Masterclass. The first of the WECAN training developments have been arranged for July in Frankfurt. Following receipt of nominations from member organisations and candidate members, the Board nominated Izabella Pawlowska and Thráinn Thorvaldsson to the Smart Start programme and Bernd Troche and Dag Utnes to the Masterclass.
 - The Board is also available to members seeking assistance and advice where requested. There has sometimes been modest financial support for specific projects.
 - During Anja Vancauwenbergh's maternity leave between March and July 2018, Judy Higgins took over the running of the Secretariat from Dublin with admirable efficiency. Judy has since obtained a post in the Irish Civil Service.

Goal 6: Support a co-ordinated European research program with patient advocate representation



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Last year we reported that progress was being made on EU funding for prostate cancer research on a co-ordinated basis. This covered the Horizon - 2020 funded study which looked at prostate cancer and Big Data. Europa Uomo was represented on the review panel in 2017 which assessed the final four bids and selected the PIONEER project. The patient interest in the PIONEER consortium is represented by our former Chairman Ken Mastris in his capacity as a Board member of ECPC [European Cancer Patient Coalition] for details of the study use the following link:

<https://www.imi.europa.eu/projects-results/project-factsheets/pioneer>

APOLLO Study Bid

The current year has seen the development of a new consortium which has entered a bid for the Artificial Intelligence – Big Data project on Quality of Life of Men with Prostate Cancer. This time Europa Uomo is part of the consortium, represented by John Dowling, which lodged its bid towards the end of April 2019. A result on the bid is expected in the autumn. The study will be funded over a 5-year time period.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The EMA is one of the main scientific calls on patient representations. The participation of Europa Uomo in EMA work groups and commissions is an important part of our work in representing prostate patient interests. The Agency recently moved from London to Amsterdam following the UK decision to leave the EU.

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- Europa Uomo is a member of the Patients' and Consumers' Working Party of the EMA. This group, representing 19 patient and consumers groups is briefed by the EMA on both organisational and scientific developments. It meets quarterly and at least one of the meetings is a joint one with the Healthcare and Professional Working Party representing the medical and allied interests. The current Europa Uomo representatives on the PCWP are André Deschamps, as principal representative, and Will Jansen as alternate. John Dowling acts as reserve.
 - All EMA scientific committees have patient representation except the Committee for Medicinal Products for Human Use (CHMP). The question of including patient representation on the CHMP is under review, but in practice the working groups and advisory groups established by the CHMP all seek to have patient representation and Europa Uomo is regularly asked to provide one or two patient representatives for such groups.

These may include an application from a company for marketing authorization;. This may be an up-front authorisation application or it may be a company looking for advice and seeking to test the views of clinicians, researchers, patients and the EMA experts as to whether their approach might be likely to receive favourable consideration. Within the European Union, health matters are the responsibility of individual member states, so the role for the EMA is therefore limited in terms of what individual states can be required to do.

- The Committee for Advanced Therapies (CAT), has two patient representatives and two alternates, one of whom is our Liaison Officer, Erik Briers, who has served three years in that capacity. The Board was pleased to support the candidature of Erik when the EMA invited applications earlier this year to serve as a full member of CAT. His candidature will be determined over the next few months. Erik has provided the short note below and a fuller report on the work of the CAT can found at Appendix 5.

The CAT is the EMA's committee responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products (ATMP's) and to follow scientific developments in the field (wording from EMA).

The final advice of the CAT is forwarded to the CHMP (Committee for Medicinal Products for Human Use) who is responsible for the final advice to the European Commission. There are several types of advanced medicinal products that each have specific rules in the regulatory tract but they all have a high level of complexity in common. The CAT committee meets every month (except in August) for three days in Amsterdam (formerly in London).

It is interesting to note that one of the first ATMP's ever to be approved by the CAT was a treatment for prostate cancer. It was the Dendreon immunotherapy PROVENGE or Sipuleucel-T (2013). Today the company Dendreon is only active in the USA and the product has been withdrawn from use in the European Union at the request of the marketing authorisation holder.

As with most of the committees, the CAT has patient representatives on board, two members and two alternates selected from proposals by patients' organisations and appointed by the European Commission for a renewable term of three years. Three years ago, Europa Uomo proposed for the first time someone to be a member of the CAT and the Commission appointed Erik to be an alternate member for a three-year period ending June 2019. For the upcoming period of three years (2019-22) Erik Briers was supported again to be a member by Europa Uomo, we await the decision of the Commission. Learn more about the CAT and see an example of an approved product in Appendix 5.

- The PRAC, the Pharmacovigilance Risk Assessment Committee, is responsible for the monitoring of side-effects of medicines that are effectively on the market. There is currently no Europa Uomo representation on this committee.

Integration of Prostate Cancer Research

- Parliamentary support has been achieved in the research funding program Horizon 2020 for Big Data. As mentioned above, the PIONEER study was inaugurated in 2018 and this year there is a new funding round for a Big Data – Artificial Intelligence study into the Quality of Life of Life of Men with Prostate Cancer. Europa Uomo is a member of one of the consortium bidding for funding for this study and is represented by John Dowling. This consortium has named its bid APOLLO and the outcome of the bid will be known in the autumn.

Patient Survey on Quality of Life for Men with Prostate Cancer

At our GA in Dublin last year a decision was taken to carry out a patient organised and conducted survey of the quality of life men of with prostate cancer. At the first meeting of the new Board in Amsterdam last July, Guenther Carl took responsibility for taking the project forward. After an intensive period of negotiation with an external survey firm and briefings for the Board followed by much debate the decision to proceed was taken at the Board on March 15th. With the final contractual matters disposed of the project was formally launched on 24 April.

This is potentially one of the most important initiatives undertaken by Europa Uomo and will have major implications, if the expectations of the 2018 GA and the Board are fulfilled. Guenther Carl will brief delegates on the project at the

GA in June. Below is a chronology showing the steps leading up to the launch of the QoL project in April this year.

Following last July's Board meeting, Guenter Carl began the scoping phase of the project. Over the summer Guenther sought advice on who could undertake such a survey for EUomo. At the September Board it was reported that a suitable UK-based company had been found and from discussions with them and some of our possible sponsors for the project it was agreed to use the established QoL survey tools EORTC 30 and EPIC 26.

From his discussions with various parties Guenther suggested a rough quantification of cost would be €50K - €75K with Europa Uomo providing the participants. At this point Guenther and his Board colleagues felt they had enough to proceed to the next step and go into details with potential sponsors.

This was done initially at the ESMO meeting with sponsors Janssen, Ipsen and Bayer. All three provided written support for the QoL project plan with pledges of € 25.000 each to cover the costs of the survey. One of the sponsors had used a firm in the UK who had done a satisfactory QoL study for them. This recommend firm proved to be Cellohealth and, by the time of the November Board meeting in Brussels, discussions had proceeded with the firm and a "First Offer" obtained. This proved to be within estimate and the Board approved the continuation of negotiations with Cellohealth and the obtaining of permissions to use EORTC and EPIC survey programmes. Having obtained permissions sought from EORTC for 22 language sets and the University of Michigan EPIC versions in German, English and French, anything else to be translated.

Before the end of December 2018, it was possible to start to draw up memoranda which would allow us engage with our sponsors to start the process within their own companies to get approval for funding. At each stage in the process the Board debated extensively the various aspects of the project, but provided the approvals need to proceed.

By the time of the January Board meeting in Brussels Janssen had been briefed about the details of the QoL drawn up and Cellohealth was informed of the actual situation with our Board and sponsors. There was a good deal of phone discussion between EUomo and our sponsor, Janssen. Before the end of that month the funding from that sponsor had arrived. By the following month Bayer confirmed that its internal discussions were looking positive. In March, this year, Ipsen confirmed financial participation as discussed. Again, the Board of

EUomo met in Barcelona, prior to discussions arranged with sponsors during the EAU congress. Shortly afterwards Guenther received a standard contract proposal from Cellohealth.

Because of the need to procure sufficient participants to make the survey results meaningful Guenther contacted our communications consultant Simon Crompton to brief him and ensure that he was integrated into the publicity campaign we will require within our membership to ensure an appropriate participation rate. The Board authorised Guenther Carl and Treasurer Ioannis Vanezos to proceed with the finalisation of the contract.

As reported above, Europa Uomo is also involved with the EAU-backed APOLLO consortium bidding for funding for a Big Data/Artificial Intelligence study into the Quality of Life of Prostate Cancer Patients. It was arranged that APOLLO would utilize the results of the EUomo survey and Prof. Monique Roobol requested some additional questions be added to the EUomo survey. This was agreed and confirmed to Cellohealth with attendant modification made to the Contract.

With all these last-minute modifications the contract was signed on 24 April and reported to the Board at its meeting on 29 April. Some outstanding funds promised are awaited. The Cellohealth will shortly be in touch with the Board to provide details of how we shall proceed.



"Instead of chasing the mailman, I've been sending him bogus text messages."

5. Funding of Europa Uomo and Financial Report

Summary:

- This report is based on our audited accounts as required by Belgian law
- No discrepancies were found during audit
- The Board continues to distribute some costs to projects
- Income equals more or less spending
- There is extra spending on two important projects

The funding of Europa Uomo comes from small contributions from member organizations through their annual dues, contributions from partner organizations, especially the European Association of Urologists (EAU) and the European School of Oncology (ESO), a number of pharmaceutical companies and reimbursement for costs where Board members or LOCs have attended meetings.

As with any organisation, but especially in one run by volunteers, it is not always possible to roll out projects to the intended timeline. As was the case last year, when comparing the budget presented in our previous annual report, some projects which were launched more slowly than expected did not reflect the full financial provision made. Hence we show less spending and less income in the actual –budget comparisons.

As we like to be cautious, our budgets for 2019 and 2020 again show ambitious spending and income. It is the Board's task to monitor and align income and spending.

Patient groups are living in a changing world. Due diligence, avoidance of conflict of interest and EMA guidelines are imposing stricter rules on those receiving funds and similarly for our sponsors.

Open bookkeeping is a key to our further success. That is why we distinguish in our budgets and reports the sponsorship given for our core activities and those for projects.

Our accounts have been audited and no problems were found. So, the statements below are a true and honest account.

In accordance with Belgian law for not-for-profit organizations it is necessary that these financial reports be considered and approved by the General Assembly so that the Board may be discharged.

Europa Uomo is compliant with the EMA guidelines on the funding of recognized patient organizations in terms of the number of pharma companies from whom it draws financial support and the requirement that it is not more than 50% dependent on any one source.



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5.1 Balance Sheet at December 31, 2018

Accounts audited by Guido Smet

ASSETS:

Bank accounts

Business Compact account	121.427,44
Savings Account	50.314,34

Provision Receivables

Pharma grants	50.000,00
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Deferred Expenses

Barcelona and Leopold hotels	7.264,00
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Total assets: 229.005,78 Euro

LIABILITIES:

Capital of Association

Capital

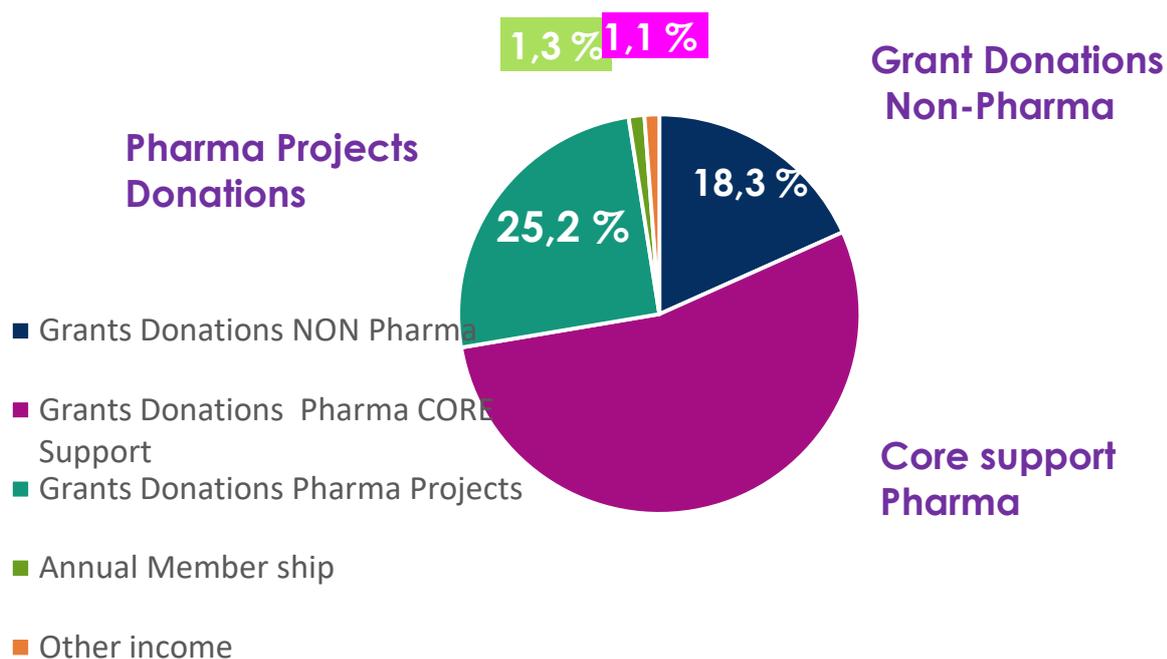
Balance at 31/12/2017	221.591,55
Transfer Balance + 10.715,25 (2018) – 3.857,27 (2017)	6.857,98

Deferred income and accrued expenses

Costs yearly accounts Guido Smet	151,25
Website maintenance	405,00

Total liabilities 229.005,78 Euro

5.2 Income 2018 distribution



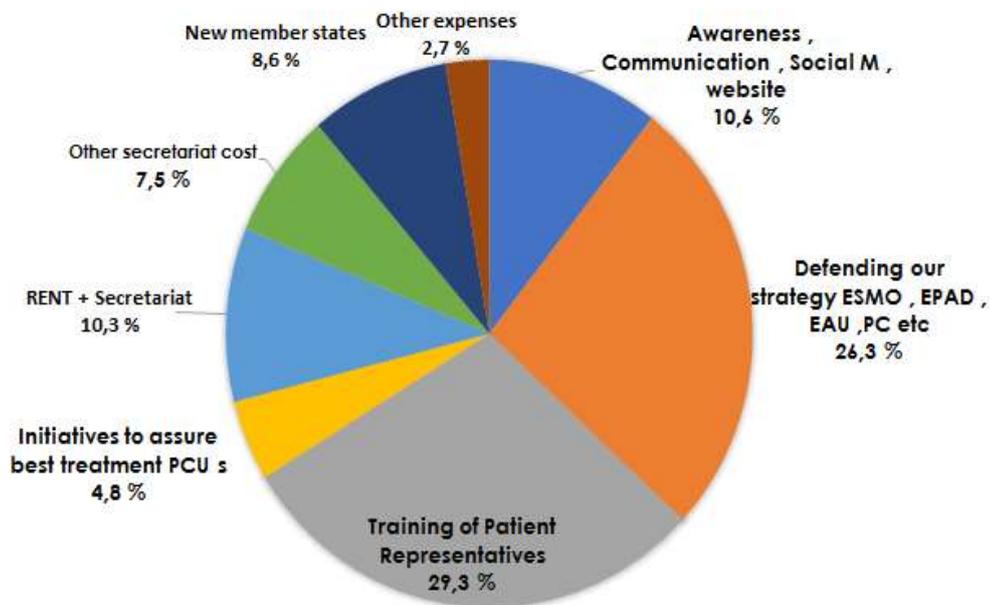
Breakdown	Value	Percentage of Total
Grants Donations non-Pharma	30.400	18,3%
Grants Donations Pharma CORE support	90.000	54,1%
Grants Donations Pharma projects	41.987	25,2%
Annual membership	2.100	1,3%
Other income	1.987	1,1%

5.3. 2018 Expenditure results on new project approach

	Projected Expenditure on New projects 2018	Actual Expenditure on new projects
Premises and secretariat	16.000	16.000
Other secretariat costs	1.000	11.649
Project 1: Awareness and Communication	22.500	16.500
Project 2: Defending our Strategy	39.000	40.950
Project 3: New member states	16.500	13.400
Project 5: Training Patient Advocates + GA/Training	55.000	45.700
Project 4: Website – amalgamated with 1		
Project 6: Audit PCUs	9.000	7.431
Internet	200	
Audit fee + fee tax return	2.500	1.010
Legal publications	150	129
Insurances	600	524
Memberships	300	
Refund travelling costs meetings	10.000	
Other meeting costs	32.000	1.918
Bank charges	250	203
Tax on assets non-profit organisations	500	343
Contingency	5.000	
Total expenditure	210.500	155.760

5.4 Distribution of 2018 Expenses on New Projects Approach

Distribution of 2018 expenses on new projects approach



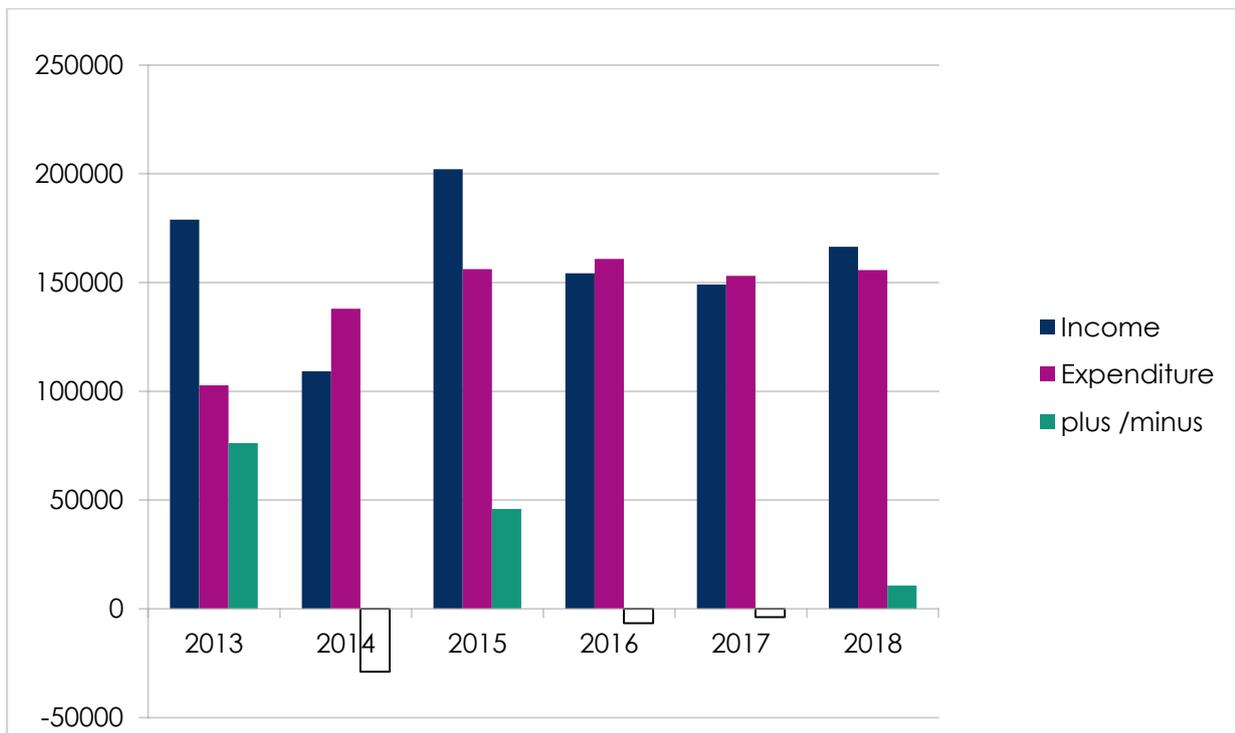
EUROPA UOM

5.5 Revenues Budget/Actual 2018 in Euro

	Budget 2018	Actual 2018
Total grants and donations non-Pharma	35.000	30.400
Total grants and donations Pharma non project-based	90.000	90.000
Non specified project-based income	10.000	0
Total grants and donations Pharma project-based	75.000	41.987
Annual membership fees 2018	2.200	2.100
Income other (Misc. Funds)		1.987
Total income	205.000	166.475

In 2017 the total grants were € 149.184 compared with a 2016 figure of €154.282.

5.6 Results for the years 2013-2018



5.7 Projects Overview

Projects	GOALS	Awareness	Screening	Treatment	New members	EU Organizatio
Awareness & Communication + Social Media		YES	YES	YES		
Defending our vision , strategy ESMO,EMA,EPAD,..		YES	YES	YES		YES
New member states		YES	YES	YES	YES	YES
Initiatives to assure best treatment (PCU audits)				YES		
Quality of Life		YES		YES		
Training of Patient representatives		YES	YES	YES	YES	YES

5.8 Three Years Revenue Budgets 2019-2020-2021

	Revised budget 2019	2020	2021
Total grants and Donations non- Pharma	40.000	40.000	40.000
Total grants and Donations Pharma non project-based	75.000	75.000	75.000
Total grants and Donations Pharma project-based	150.000	90.000	90.000
Annual membership fees	2.200	2.200	2.300
Income other (Misc. funds)	3.000	3.000	3.000
New Member Support	5.000	10.000	15.000
Total income	275.200	220.200	225.300

5.9 Three years projected expenditure per budgets 2019–2020-2021

	2019	2020	2021
Premises and secretariat	16.000	16.000	16.000
Other secretariat costs	1.000	1.000	1.000
Projects			
1 Awareness + Communication + Social Media + Website	22.500	22.500	22.500
2 Defending our strategy (ESMO, EU, EPAD, EAU, etc.)	40.000	40.000	40.000
3 New member states	16.500	16.500	16.500
4 New: Quality of Life Survey	75.000	12.000	12.000
5 Training Patient Advocates and Activists	55.000	55.000	55.000
6 Initiatives to ensure best treatment – PCUs	44.000	44.000	44.000
Internet	200	200	200
Audit fee and tax	2.500	2.500	2.500
Legal publications	150	150	150
Insurances	600	600	600
Memberships	300	300	300
Other meetings costs	11.000	11.000	11.000
Bank charges	250	250	250
Tax on assets as a non-profit organisation	500	500	500
Contingency	5.000	5.000	5.000
Total: 215.500	290.500	227.500	227.500

6. Conferences & Meetings Attended

Members of the Board and Liaison Officers attend a wide range of meetings on behalf of Europa Uomo. During the course of the year the meetings attended have been reviewed and the Board will now only attend as a Board: the EAU congress, PCa18 and following PCa conferences, EPAD meetings and the GA. Whenever the Board needs to convene away from the above conferences and meetings it will try to do so by teleconference.

Most meetings attended by EUomo are either with other patient organisations, with the representatives of scientific and professional bodies and meetings with sponsors, and administrative personnel in the Commission, EMA and similar bodies. A listing of meetings and conferences attended by Europa Uomo representatives is set out in Appendix 4 to this report.

7. Conclusion

Europa Uomo's tagline "The Voice of Men with Prostate Cancer in Europe" continues to hold. This report is evidence of the continuing development of our organisation and its influence within the European-level institutions, patient organisations, professional organisations and industry supporters. We are a confederation of prostate patient support organisations, we seek to build on the progress of the past 16 years since our foundation. We do not apologise for repeating in this Report that this has been achieved as a result of the efforts of a relatively small cohort of volunteers elected by successive General Assemblies together with the Liaison Officers and our *ex-officio* members.

We repeat once again in this conclusion that **"it is not enough that the aims of our organisation are worthwhile and that there is a real need to be met on behalf of prostate cancer patients all across Europe. To be effective and to develop requires the correct strategy and the effort to realise it."**

The Board wishes to thank all those who have made their effort to develop and further the organisation.

Approved by the Board May 2019

Appendix 1

Membership Development – Project Central & Eastern Europe

Aim: To encourage new support groups in European States

The provision of effective patient support organisations is very uneven in mainly eastern and central European states. For the past few years Europa Uomo has been seeking to establish an active presence in the region which would improve the provision for prostate patients and to build appropriate relations with professional groups in these countries.

With the warm assistance of our Gladiator member organisation in Poland the Board was able to make a significant step forward in 2017/18 with the recruitment of a Prostate Cancer Patient Officer, Izabella Pawlowska, who is based in Warsaw. This post has been effective since the beginning of March 2018.

Two Board members, Stig Lindahl and Pentti Tuohimaa are working with Izabella. For the moment effort is being concentrated in Estonia, Latvia and Armenia. Other leads are being followed up with contacts to Europa Donna and Cancer Association in the region for later development. Representatives for the Healthcare providers are also contacted. The work is planned and followed up with weekly Skype conversations.

Estonia (Existing member)

Since 2016 Kalev Lehtla was chairman of the Estonia Patient organisation. During November that year he had to give up his fight against the cancer and the work started to find a replacement.

Both Pentti Tuohimaa Finland and the Finish PROPO headed by Kimmo Järvinen started to reinforce the local Estonian organization both with training in Finland and by a cooperation between Åbo University Hospital in Finland and Tartoo University Hospital in Estonia. The Estonia Cancer Association (Vivian Vulp) was also involved to find a replacement. Niilo Saard was willing to help us to rebuild the Prostate cancer organization. Niilo Saard was unfortunately also affected by his disease and left us in the beginning of 2019. The work has now to start again.

Latvia (New member)

After some contacts were made, Izabella found a group headed by Helmut Bekis that was willing to start up a patient organization in Latvia. Izabella visited Riga in

November to follow some of the local activities and a press conference. Discussion concerning how to organise a patient organization and how to become a member of EUomo was also on the agenda.

After some months of email communication, where an action plan was defined, Stig Lindahl went to Riga to assist in the final preparation. The organisation structure was defined in April and the members of the board identified. The application from Latvia was received at the end of April.

Armenia (New member)

Background: After some initial Skype conversations in the beginning of 2018 it was decided to arrange a common conference for Europa Donna and EUomo in May 2018. In the meantime John Dowling supported Armenia with all needed information to start up a patient organization and how to become a member of EUomo. Due to some political turbulence in Armenia the conference had to be postponed to November.

The May conference was finally staged in the beginning of November 2018. Stig Lindahl attended and gave information to the conference on the theme "To live with Prostate cancer in different parts of Europe". During the visit a number of meetings were held to define the plan ahead and also a meeting with the local Prime Minister in Artsakh took place. An application has been received and was discussed and approved by the EUomo Board meeting in Barcelona. Final decision at GA in June.

Iceland (New Member)

After a period of initial contact with Skuli Jon Sigurdarson a new contact was found in Iceland, Thráinn Thorvaldsdsson, who has been involved in supporting group for Active Surveillance for a long time. Thráinn had, together with some friends in the US, tried to arrange a conference in Reykjavik during 2019. The funding does not seem to be available. He is now cooperating with Jon to establish a Patient organisation Framför (Progress) in Iceland. The application was received in mid-April and will be placed before the GA in June.

Preparation for 2019

During 2018, a number of countries has been contacted via Europa Donna, to indicate our interest to find potential patient organisations for further negotiations. Targeted countries have high incidence and mortality rates for prostate cancer. We are looking especially at the Balkan region.

It is also important to support a closer cooperation between members in regional areas. The Nordic countries have, for many years, learned a lot from each other in regular meetings to exchange information. By including Iceland in the group all members will gain a lot. Similar constellations can be started in the Baltic area and in the future also in the Balkan region. “**Regional Patient Awareness Days**” where we share new information available. The regional healthcare providers should play an important role in those events.

Stig Lindahl and Team



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Appendix 2 WECAN Training Programme

SmartStart - Starting and Building a National Non-Profit Patient Group

3-day course for patient advocates

- who are in the process of starting a group/organisation
- who have already started an organisation and are seeking to improve their skills
- who are relatively new in existing groups/organisations and who would like to take future responsibility as Chair, Board Member or Director

The 3-day training course provides...

- **basic knowledge to set up and maintain a national cancer patient group** in their own country
- **networking with experienced patient group leaders and trainers**
- **balanced mix of practical advocacy and support “tools”**

Main topics:

- **Building A National Non-Profit Patient Group** (Strategic planning, legal aspects, governance, financial aspects, marketing)
- **Cancer World: Relationships and working within the system** (clinical research, working with volunteers/physicians/industry/media, healthcare system processes)
- **Best practices and personal skills** (patient meetings, making medical content understandable, presentation/moderation skills, online tools)

WECAN/ESO Masterclass in Cancer Patient Advocacy

■ 3-day Masterclass for experienced patient advocates

Help participants hone their advocacy and leadership skills

Discuss ways of improving organizational impact and effectiveness

Review state-of-the-art approaches to evidence based advocacy

- Provide participants with opportunity to network and share experiences

Main topics (2018):

Lobbying for change

Building effective and sustainable

EU cancer patient networks

(leadership, evaluating effectiveness,

challenges of working with industry,

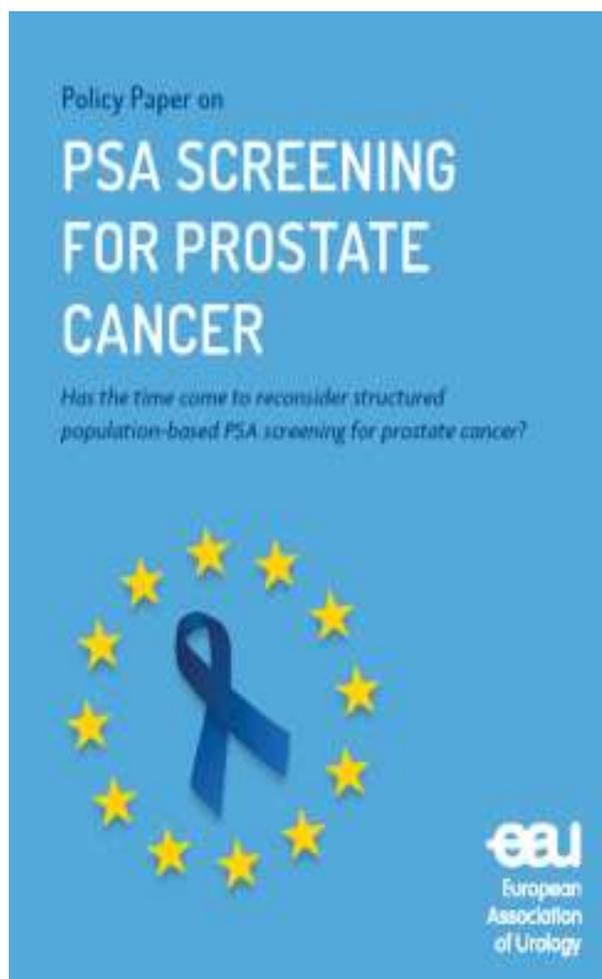
Community Advisory Boards)

Achieving access to affordable medicines

Developing advocacy leadership skills (Communication, persuasion & influence, coaching, interpreting scientific data)

Moving from anecdotal to evidence-based advocacy

Appendix 3



1. Executive Summary

INTRODUCTION: WHY THIS PAPER NOW?

Prostate cancer (PCa) is the most commonly diagnosed cancer in men, with more than 417,000 new cases and 92,000 deaths in Europe recorded each year. Last year, registry data have shown that death from prostate cancer has overruled death from colorectal cancer being the second most cause of cancer-related death in men behind lung cancer. Despite this significant public health burden, relatively little is performed on prostate cancer screening at EU level, particularly in comparison to breast, cervical and colorectal cancers.

- **Recent evidence demonstrates the efficacy of prostate cancer screening**

The European Randomised Study of Screening for Prostate Cancer (ERSPC) demonstrates that PSA screening reduces disease specific mortality by 21%, which is equivalent to one death prevented per 781 men invited for screening or one per 27 prostate cancer detected. The evidence shows that after 20 years of follow-up the number of patients needed to screen and diagnose prostate cancer decreased to 101 and 13, respectively, to prevent one prostate cancer death. As such, PSA screening results in mortality reduction are obviously better than in breast or colon cancer screening.

- **Worrying statistics on prostate cancer mortality where prostate cancer screening has been cut back**

Key evidence has emerged from two independent studies in 2017 and 2018 to demonstrate that a lack of prostate cancer screening is reversing the trends

of declining death rates. Since practitioners in both the UK, and the USA have been advised not to perform PSA for early detection, worrying statistics are emerging to demonstrate that cancer mortality is increasing.

• **Quality of Life**

Where mortality rate is always considered in screening options, the quality of life of a patient is seldom taken into account. Early treatment for prostate cancer lowers the risk of incontinence and impotence significantly, while treatment at metastatic phase has a negative effect on the quality of life. Hence, there is a big opportunity to improve the quality of life if early detection is achieved in combination with avoidance of overtreatment.

• **The availability of gold standard good practice and emerging new technologies**

Since PSA screening ultimately reduces the rate of men with metastatic PCa at diagnosis and, in turn, mortality, different organisations have reconsidered their views on screening. The European Association of Urology (EAU) released its recommendations on early detection in the year 2013.

At the same time, individualised risk-adapted screening strategies, as well as mpMRI and biomarkers to select candidates for prostate biopsy will reduce the risk of overdiagnosis which has been a concern in the past. Moreover, the adoption of active surveillance as an option in patients with low-risk decreases overtreatment.

2. Introduction

WHAT SHOULD THE EU DO?

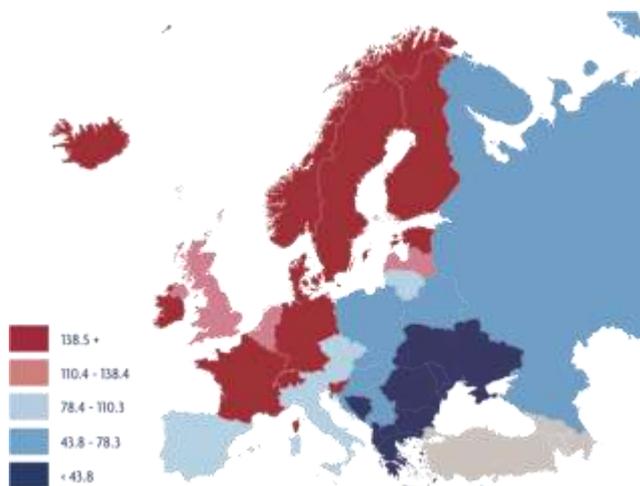
The European Union can no longer continue to overlook the most common cause of cancer and the second most

common cause of death from cancer in men in Europe. Urgent action is required to ensure the new Commission is mandated to support EU Member States in prostate cancer screening in their national cancer plans.

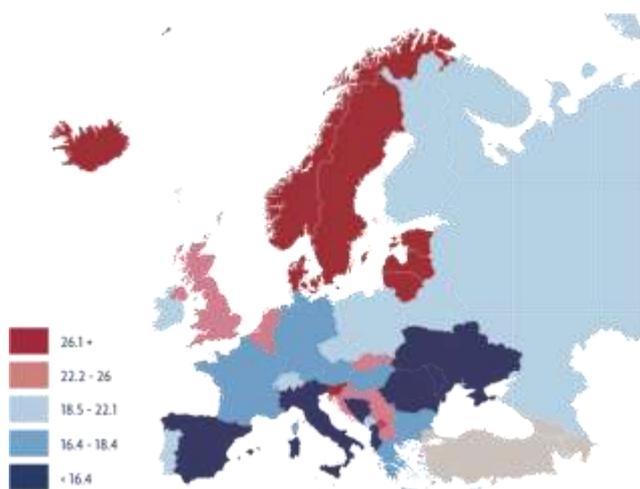
- The 2003 Council Recommendations on population-based screening need to be urgently reviewed, with prostate cancer added to the list of cancers to be addressed.
- Member States should already support a policy update on prostate cancer screening through their work on the EU Joint Action, the Innovative Partnership for Action Against Cancer (IPAAC)
- MEPs should ensure that European action on Prostate Cancer screening is included in the group manifestos as they prepare for European elections
- The new college of Commissioners mandated in 2019 should be empowered by the European Parliament and Member States to support Member States with European guidelines on prostate cancer screening.
- Member States should also bring good practice on prostate cancer screening to the Steering Group on Health Promotion, Disease Prevention and Management of non-communicable diseases, where the European Commission can assist in channelling necessary support and funding at EU level.

Prostate cancer is the first most frequently diagnosed solid cancer and the second most common cause of cancer death among European men with more than 450,000 new cases and 107,000 deaths expected in 2018 in Europe. Prostate cancer is characterised by slow development when diagnosed at an early stage. Conversely, it is almost always too advanced to be cured when diagnosed late. The need for more

extensive surgical approaches and/or hormonal or chemotherapies is associated with a negative impact on quality of life in men with advanced disease as compared to those men diagnosed at an early stage.



Estimated incidence prostate cancer in men, 2012



Estimated mortality from prostate cancer in men, 2012

The treatment of advanced and metastatic disease is very costly and only marginally improves survival. While the costs of robot-assisted radical prostatectomy, which is one of the most used treatments for early prostate cancer, does not exceed €15,000 per patient, the costs for the management of patients with castration-resistant, non-curable PCa can be estimated in approximately €140,000 per patient per

year up to €300,000 during a patient's lifetime in Western countries.

PSA stands for Prostate Specific Antigen, which is a protein that can be measured in the blood of men. Elevated PSA levels might be detected in men with prostate cancer and PSA has been proposed as a biomarker or indicator¹. Screening based on PSA allows for the detection of PCa at an early stage, reducing cancer-specific mortality at long-term follow-up. Nonetheless, many of the tumours detected by PSA develop slowly and men would not have experienced any symptoms during their lifetime¹.

Given the risk of overdiagnosis (and overtreatment) associated with screening, in the year 2012 the US Preventive Services Task Force released a recommendation against its use. The consequence of the release of these recommendations was a reduction in PSA-based screening. This led to more men with advanced PCa and a tendency towards higher prostate cancer death rates.

Member States have so far mandated the European Commission to support population-based screening programmes for breast, colon and cervical cancer, while prostate cancer screening has been overlooked.

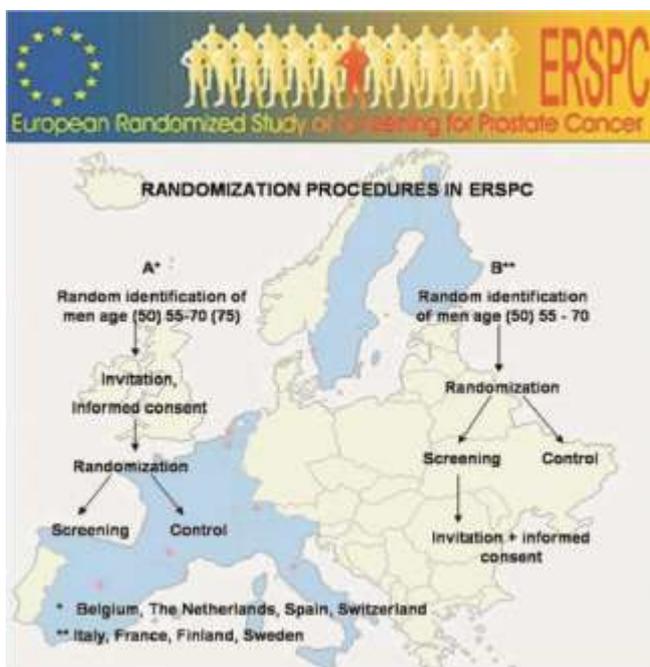
Due to recent developments, the Commission has proposed the EU's Joint Action on Innovation Partnership in Action Against Cancer as the best place to start the policy work on a possible inclusion of prostate cancer screening programmes in the National Cancer plans

http://www.europarl.europa.eu/doceo/document/E-8-2017-007165-ASW_EN.html

3 Is PSA-based screening reducing mortality?

New evidence proves it is

The implementation of structured screening programmes based on repeated measurements of PSA leads to the detection of prostate cancer at an early stage, improving our ability to cure the disease. This reduces the risk of metastases during follow-up and of dying from the disease itself. The evidence assessing the role of screening based on multiple PSA testing rounds is dominated by two randomised trials.



The European Randomised Study of Screening for Prostate Cancer (ERSPC) randomised 182,000 men aged 50 to 74 years to PSA screening every 4 years vs. control¹. At 13-year follow-up, PSA screening reduced disease-specific mortality by 21%, which is equivalent to one death prevented per 781 men invited for screening or one per 27 prostate cancer detected. After almost 20 years of follow-up the number of patients needed to screen and diagnose decreased to 101 and 13, respectively, to prevent one prostate cancer death. In comparison, for diagnosing breast

cancer the numbers needed to screen vary between 111 and 235, while for diagnosing colon cancer is 850. Therefore, PSA screening with comparable follow-up is even more effective compared to breast or colon cancer screening.

The second trial was the prostate arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO), which randomised more than 76,000 men to annual PSA testing for 6 years vs. usual care. After 17 years of follow-up, no differences in mortality were detected between the two arms. However, one out of two men had undergone at least 1 PSA test before randomisation. Moreover, up to 80% of men in the control group reported having undergone at least 1 PSA test during the trial. As such, this study should be considered as the comparison between organised vs. opportunistic screening rather than an assessment of PSA screening. Recent analyses accounting for differences in the two studies suggest that the efficacy of screening in the PLCO setting might be consistent with what was observed in the ERSPC trial.

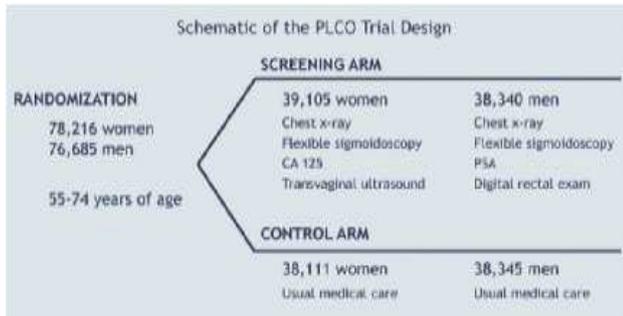
4. Concerns on Overdiagnosis and Overtreatment

Despite this compelling evidence on the efficiency of PCa screening, the medical community has historically been divided because of the risk of overdiagnosis and overtreatment.

Overdiagnosis is defined as the detection of a disease in men who don't experience any symptoms at the moment of detection and would not develop any symptoms during their lifetime if not identified by early detection activities. The risk of overdiagnosis has been estimated to be as high as 40% in screen-detected prostate cancer and is

particularly important given the slow development of the disease itself. Overdiagnosis applies particularly to older men or those with lower PSA values, where the beneficial effect of treatment is limited.

Although PSA screening reduces the risk



of mortality, its main drawback is a substantial number of unnecessary biopsies and detection of insignificant cancers, which could lead to overtreatment.

The issues related to overdiagnosis and overtreatment were the main drivers for the strong recommendations against PSA screening released by the United States Preventive Services Task Force in the year 2012. Do these concerns remain valid?

The EAU believes there are reasons why these concerns need to be readdressed and reviewed:

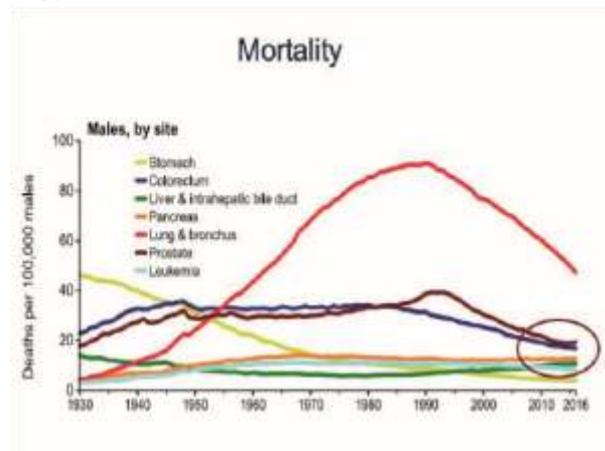
4.1 THE CONSEQUENCES OF NOT PERFORMING PSA SCREENING

Recent studies demonstrate that cutting back on PSA screening has a direct correlation with a rise in mortality rates from Prostate Cancer:

1. In many European countries general practitioners and patients were informed not to perform PSA for early detection. In the United Kingdom, 4 out of 10 prostate

cancer diagnoses are currently diagnosed at a locally advanced or metastatic stage.

2. In the United States, after a documented long decline of death rates of prostate cancer, prostate cancer mortality is increasing for the 1st time since early 1990. This has happened in parallel with PSA screening decline, where a decrease by 1018% of screening rates has been observed in recent years. Moreover, an increase in the number of patients with metastatic and advanced disease has been observed at the same time.



4.2 EARLY DETECTION OF PROSTATE CANCER RECOMMENDATION ARE AVAILABLE

Since PSA screening ultimately reduces the rate of men with metastatic PCa at diagnosis and, in turn, mortality, different organisations have reconsidered their views on screening. The European Association of Urology (EAU) released its recommendations on early detection in the year 2013. The panel recommended that a baseline PSA level should be obtained at the age of 40-45 years to initiate a risk-adapted follow-up with the purpose of reducing metastatic prostate cancer and mortality. Screening should then be offered to well-informed men with a life expectancy ≥ 10 years and the intervals for screening should be adapted according to the baseline PSA obtained at the age of 40-45 years. The American Urological Association (AUA) guidelines on screening recognise that the decision to undergo PSA screening involves weighing the potential

benefits and harms and strongly recommends shared decision-making for well-informed men aged 55 to 69 years. An interval of two years or more may be preferred over annual screening to reduce the risk of overdiagnosis and overtreatment.

The US Preventive Services Task Force updated their 2018 version and recommends to leave the choice of PSA-based screening in well-informed men between the age of 55 to 69 years up to an individual decision. However, they discouraged the use of screening in men at the age of 70 and older, where the potential benefits of PSA screening do not outweigh the harms.

4.3 NEW AND EMERGING TECHNOLOGIES AND PRACTICES ARE GAME CHANGERS IN REDUCING THE RISK OF OVERDIAGNOSIS AND OVERTREATMENT

Measures aimed at minimising the risk of overdiagnoses and overtreatment while maximising the benefits of PSA screening in terms of reduction of prostate cancer mortality are urgently needed.

INDIVIDUALISED PSA-BASED SCREENING

First, PSA should be considered in the context of other clinical characteristics such as age, family history, digital rectal examination and prostate volume. Several risk calculators that take other variables into account, have been developed and their use increases the diagnostic accuracy of PSA alone.



Secondly, one single assessment of PSA values has limited value as PSA values can fluctuate. In this context, a baseline

PSA obtained at the age of 40-45 years should be considered for risk stratification of future screening intensity.

Finally, the use of PSA screening should be discouraged in men with a short life expectancy, where the risk of dying from other causes is higher than cancer mortality.

MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING (mpMRI) BEFORE PROSTATE BIOPSY

The availability of mpMRI substantially changed the diagnostic paradigm of localised prostate cancer. MRI images are characterised by a high sensitivity and negative predictive value for aggressive disease. At the same time, it systematically overlooks insignificant prostate cancer. Therefore, mpMRI has been proposed as a first test to identify men with elevated PSA levels who should be considered for a prostate biopsy.

The use of mpMRI before prostate biopsy would allow for the detection of a higher proportion of significant prostate cancers compared to random biopsies. This would lead to a reduction of more than 10% of diagnosing insignificant diseases and of 30% in the number of unnecessary biopsies. The implementation of screening strategies that include mpMRI would avoid a substantial number of unnecessary prostate biopsies and other disease diagnoses.

NOVEL MOLECULAR TESTS

Different molecular biomarkers have been proposed to identify men with significant prostate cancer. These tools based on algorithms including PSA or other proteins and clinical information can identify clinically significant disease with high accuracy and might further decrease the risk of overdiagnosis.

Nonetheless, they should not be considered as alternatives to PSA screening and should not be used as reflex tests. They provide complimentary information that enhance prediction of high-grade prostate cancer. Their integration with other tools such as mpMRI might ultimately reduce the number of unnecessary biopsies without increasing the risk of missing a significant disease.

ACTIVE SURVEILLANCE FOR MEN WITH LOW RISK PROSTATE CANCER

Well-selected men with low-risk prostate cancer might be included in active surveillance programmes with the aim of reducing the risk of overtreatment without losing the window of curability. Patients managed with active surveillance receive periodic assessments with PSA measurements, digital rectal examination, mpMRI, and eventually prostate biopsies. Treatment starts as soon as the aggressive but still curable disease is detected in men with an adequate life expectancy.

This approach reduces treatment-related side effects like urinary incontinence and erectile dysfunction in up to 65% of patients with low- or intermediate-risk disease at 15-year follow-up. As a consequence, active surveillance is currently recommended by the European Association of Urology for the management of all men with low-risk prostate cancer with an adequate life expectancy.

5 Conclusions – urgent action required!

The European Union can no longer continue to overlook the most common cause of cancer in men in Europe which developed to be the number two cancer killer in men. Urgent action is required to

ensure the new Commission is mandated to support EU Member States in prostate cancer screening in their national cancer plans.

The implementation of PSA-based screening at a European level to decrease prostate cancer mortality and improve Quality of Life should be discussed again in the light of the current evidence and should be included in the policy agenda of the European Commission. IPAAC is a possible vehicle to introduce a policy update on prostate cancer screening.

The 2003 Council Recommendations on population-based screening should be updated to include Prostate Cancer. The new European Commission should be mandated by this or other mechanisms by the European Parliament and EU Member States to produce guidelines on Prostate Cancer Screening to support EU Member States.

The EAU Guidelines could form the foundation of these recommendations as they are evidence-based and developed from a multidisciplinary point of view.

EU Member States should also bring good implementation practice on Prostate Cancer Screening to the Steering Group on Health Promotion, Disease Prevention and Management of noncommunicable diseases. This in turn should encourage the European Commission to channel appropriate support and funding to Prostate Cancer screening and research.

Let's use the opportunity of new elections and a new Commission to ensure that Prostate Cancer is given the priority at EU level that is needed!

Please note the abridging of this paper due to space consideration. Most of the deleted

material consists of published references relating to the content of the policy paper.

For the full list of references please access the paper on EAU website:

www.epad.uroweb.org/missionvision/white-paper

Mother/Wife Knows Best?



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Appendix 4: Activities List June 2018 – May 2019

C. Arnold, A. Deschamps, J. Dowling, J. Higgins, W. Jansen, S. Lindahl, K. Mastris, P. Tuohimaa Europa Uomo Board Meeting Malahide, Ireland	08.06.18	T. Hope, G. Slattery, H. Wolinsky, T. Thorvaldsson, S. Lindahl Skype conversation on 'Active Surveillance'	02.08.18
C. Arnold, D. Ask, G. Battaglia, J. Blazek, H. Boogh, F. Brennan, E. Briers, E. Büchler, S. Crompton, R. Cuypers, A. Deschamps, J. Domingos, H. Donjem, J. Dowling, N. Einer-Jensen, T. Estapé, I. Gaál, J. Goncalves, J. Higgins, W. Jansen, O. Jensen, V. Kappak, B. Kavanagh, J. Kilaite, V. Koprda, S. Lindahl, M. Lippuner, K. Mastris, I. Pawlowska, L. Pecenka, W. Priesmycki, P. Rakštys, N. Saard, E. Svetlovska, H. Tavio, P. Tuohimaa, I. Vanezos, S. Voniatis, A. Wagstaff, T. Wlodarczyk, R. Wotton Europa Uomo General Assembly Europa Uomo Training Patient Advocates Malahide, Ireland	08-09.06.18	P. Tuohimaa Patient Forum Tampere, Finland	14.08.18
P. Tuohimaa Estonian PCa Patient organization meeting Tallinn, Estonia	12.04.18	E. Briers European Association of Urology (EAU) Guidelines Committee meeting Amsterdam, the Netherlands	31.08-02.09.18
E. Briers EMA Committee for Advanced Therapies (CAT) Meeting London, UK	20-22.06.18	T. Hope, T. Thorvaldsson, S. Lindahl Skype conversation on 'Active Surveillance'	02.09.18
A. Deschamps General Assembly Oncology Centre Antwerp Antwerp, Belgium	26.06.18	I. Vanezos Anticancer meeting Nicosia, Cyprus	04.09.18
E-G. Carl, A. Deschamps, J. Dowling, J. Higgins, W. Jansen, S. Lindahl, P. Tuohimaa, I. Vanezos Europa Uomo Board Meeting Amsterdam, the Netherlands	05.07.18	J. Dowling EMA Scientific Advisory Group (SAG) meeting London, UK	06.09.18
E. Briers EMA Committee for Advanced Therapies (CAT) Meeting London, UK	18-20.07.18	E. Briers European CanCer Organisation (ECCO) 2018 European Cancer Summit: 'From Science to Real-Life Oncology' Vienna, Austria	07-09.09.18
J. Dowling European Society for Medical Oncology (ESMO) Patient Guide Review Conference Call	24.07.18	E. Briers EMA Committee for Advanced Therapies (CAT) Meeting London, UK	12-13.09.18
		K. Mastris EMA Committee for Advanced Therapies (CAT) interested parties meeting London, UK	13.09.18
		E-G. Carl, A. Deschamps, J. Dowling, W. Jansen, P. Tuohimaa, A. Vancauwenbergh, I. Vanezos Board meeting Europa Uomo Milan, Italy	13.09.18
		E. Briers, E-G. Carl, A. Deschamps, J. Dowling, W. Jansen, P. Tuohimaa, I. Vanezos PCa18 2nd EAU Update on PCa Milan, Italy	14-15.09.18

J. Dowling Telephone conversation Kieran Kenny (Genomic Health) 17.09.18	A. Deschamps Janssen Patient Board meeting Brussels, Belgium 06-07.11.18
A. Deschamps Phone conversation Dr. Upal Kasari (Bayer) 21.09.18	E. Briers, W. Jansen 10th European Multidisciplinary meeting in Urological Cancers (EMUC) Amsterdam, The Netherlands 7-11.11.18
A. Deschamps EMA PCWP plenary meeting & PCWP/HCOWO joint meeting London, UK 25.09.18	S. Lindahl Seminar Europa Donna – Europa Uomo Yerevan, Armenia 08.11.18
J. Dowling Janssen Patient Advisory Board meeting Amsterdam, The Netherlands. 09.10.18	E-G. Carl, A. Deschamps, J. Dowling, W. Jansen, S. Lindahl, A. Vancauwenbergh, I. Vanezos Board meeting Europa Uomo Brussels, Belgium 14.11.18
A. Deschamps, A. Vancauwenbergh, N. Verbrugghe Meeting on the communication report of Simon Crompton Antwerp, Belgium 10.10.18	P. Tuohimaa Patient Forum Tampere, Finland 21.11.18
E. Briers EMA Committee for Advanced Therapies (CAT) Meeting London, UK 10-12.10.18	A. Deschamps IPSEN Advisory Board Les Ulis, France 22-23.11.18
S. Lindahl Yearly seminar Finnish Cancer Association Helsinki, Finland. 12.13.10.18	W. Jansen 2nd European Alliance for Personalised Medicine (EAPM) meeting Milan, Italy 26-28.11.18
I. Vanezos Meeting with the Committee of Ministry of Health Cyprus for EU visions and targets Nicosia, Cyprus 19.10.18	E. Briers EMA Committee for Advanced Therapies (CAT) Meeting London, UK 5-7.12.18
E. Briers European Society for Medical Oncology (ESMO)18 Annual Congress Munich, Germany 19-22.10.18	A. Deschamps Extraordinary General Assembly Oncology Centre Antwerp Antwerp, Belgium 11.12.18
A. Deschamps, I. Vanezos, E.G. Carl WECAN meeting ESMO 18 annual congress Meetings with various sponsors/partners Munich, Germany 21-23.10.18	A. Deschamps Meeting Astellas Antwerp, Belgium 11.12.18
A. Deschamps 1st ECCO Policy Workshop on Multidisciplinary Cancer Care: "Essential requirements to improve oncology outcomes" Brussels, Belgium 31.10.18	A. Deschamps, I. Vanezos AstraZeneca Global Virtual Advisory Board meeting for Patient Advocacy Leaders 14.12.2018
I. Pawlowska Movember meeting Riga, Latvia 01-03.11.18	A. Deschamps New Year reception OCA Antwerp, Belgium 14.01.19
	J. Dowling WECAN meeting on Training Milan, Italy 15-16.01.19

I. Vanezos
Meeting Health Ministry Organisation: The new health plan of Cyprus
Nicosia, Cyprus 17.01.19

E-G. Carl, L. Denis, A. Deschamps, J. Dowling, S. Lindahl, P. Tuohimaa, A. Vancauwenbergh, I. Vanezos
Board meeting Europa Uomo
Brussels, Belgium 21.01.19

A. Deschamps, I. Vanezos
Meeting IPSEN
Brussels, Belgium 22.01.19

E-G. Carl, A. Deschamps, J. Dowling, W. Jansen, S. Lindahl, P. Tuohimaa, I. Vanezos
European Prostate Awareness Day (EPAD)
Brussels, Belgium 22.01.19

E. Briers
EMA Committee for Advanced Therapies (CAT) Meeting
London, UK 23-25.01.19

J. Dowling, S. Lindahl, I. Pawlowska, A. Vancauwenbergh, N. Verbrugghe
Skype meeting Editorial Board 13.12.19

A. Deschamps, I. Vanezos
Visit to Europa Uomo Cyprus Loose Tie week
Nicosia, Cyprus 13-16.02.19

E. Briers
EMA Committee for Advanced Therapies (CAT) Meeting
Amsterdam, The Netherlands 20-22.02.19

S. Lindahl
Support new patient group 'Latvia'
Riga, Latvia 23-25.02.19

P. Tuohimaa
Patient Forum
Tampere, Finland 31.02.19

E. Briers
European Association of Urology (EAU) Guidelines Committee
Amsterdam, The Netherlands 11-12.03.19

E. Briers, E-G. Carl, J. Dowling, W. Jansen, S. Lindahl, I. Pawlowska, P. Tuohimaa, A. Vancauwenbergh, I. Vanezos
European Association of Urology (EAU) annual congress
European School of Oncology (ESO) 6th Observatory on Prostate Cancer 15.03.19

Board meeting Europa Uomo 15.03.19
EAU Patient Information session 17.03.19
Meetings with various sponsors/partners
Barcelona, Spain 15-19.03.19
FEFOC-EUomo Patient Forum 19.03.19

E. Briers
EMA Committee for Advanced Therapies (CAT) Meeting
Amsterdam, The Netherlands 20-22.03.19

E. Briers
EMA Committee for Advanced Therapies (CAT) Meeting
Amsterdam, The Netherlands 15-17.04.19

E-G. Carl, L. Denis, A. Deschamps, J. Dowling, W. Jansen, S. Lindahl, P. Tuohimaa, A. Vancauwenbergh, I. Vanezos
Board meeting Europa Uomo
Antwerp, Belgium 29.04.19

W. Jansen
European Medicines Agency (EMA): Scientific advice working party
Amsterdam, The Netherlands 13-16.05.19

A. Deschamps
Annual General Meeting European Cancer Patient Coalition (ECPC)
ECPC Working group on urological cancer meeting
Brussels, Belgium 7-9.06.19

Publications

A. Deschamps
Prostate cancer: time for a new European-wide strategy
Health Europa Quarterly, February 2019; 8: p.134-135

Appendix 5



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Europa Uomo and the CAT – Report by Erik Briers PhD

Introduction

For the last three years Europa Uomo supported me to be an alternate member of the Committee for Advanced Therapies. As members of Europa Uomo you could wonder why we are there and if this is important for us or for patients in general. In this report I will try to answer these questions and give some examples of approved advanced therapeutic medicinal products.

What are advanced therapeutic medicinal products (ATMP's)?

As we all know, medicines can be extremely complicated, think of chemotherapeutic products like docetaxel or cabazitaxel, both products derived from tree-leaves (European taxus tree, a very poisonous tree). Some antibiotics are also chemically very complex to isolate and to produce, but this does not make them “advanced”. On the same note, antibodies, like Herceptin or trastuzumab used in the treatment of some forms of breast cancer, are very complex, but are not ATMP's.

The EU regulation (1394/2007) on ATMP's states that “New scientific progress in cellular and molecular biotechnology has led to the development of advanced therapies such as *gene therapy, somatic cell therapy and tissue engineering...*” defines what ATMP's are. Because these products are so new, the regulation is important and defines specific rules that will govern market authorization and other matters. Similar rules are used in the US by the FDA, in Canada and Japan.

The ATMP's are seen as falling into three groups,

- [1] gene therapy medicinal products,
- [2] somatic cell therapy medicinal products and
- [3] finally tissue engineered products.

Gene Therapy Medicinal Products (GTMP) contain a recombinant nucleic acid sequence. When administered to the patient GTMPs will regulate, repair, replace add or delete a genetic sequence. The therapeutic effect must be directly linked to the recombinant nucleic acid sequence or to the product of its expression. In other words, a GTMP is a medicine that contains a sequence of genetic material that can act by itself or that can act after it has been transcribed into a protein.

Somatic cell therapy medicinal product (SCTMP) are composed of cells or tissues that have been subjected to significant treatment and/or alterations. In the person receiving the product it will have a physiological effect, intended to treat a disease. These products can be derived from donors or from the recipient himself or herself.

A tissue engineered medicinal product (TEMP) consists of engineered cells or tissues that can be of human or animal origin. These products are used with a view to the regeneration, repair or replacement of human tissue.

Classification of ATMP's is very important and it is the first step in the registration of a new medicinal product. There are many discussion issues at the CAT just because these products are so new. To distinguish between a SCTMP and a TEMP which are both derived from human (or animal) sources is not always simple and if there are no viable cells present in TEMP's, they are not classified as ATMP's at all.

For which diseases are ATMP's used?

There is no link between diseases and ATMP's and vice versa, any disease can eventually be treated with an ATMP.

But, there are some areas where it is more obvious that ATMP's are used. Some examples:

Gene Therapy Medicinal Products (GTMP)

Congenital genetic disorders, because of a defective-gene, patients suffering from these diseases could lack an important enzyme or other protein with devastating consequences.

An examples of such a disease is "**Lipoprotein Lipase Deficiency (LPLD)**" an ultra-rare genetic disorder. Lipoprotein lipase is an enzyme produced in the pancreas and needed for the digestion of some lipids. In the absence of normal lipoprotein lipase (LPL) patients suffer from repeated cases of acute and very painful pancreatitis. These patients can eventually be helped by replacement therapy where the correct lipoprotein lipase is administered, this therapy is very costly (around €300.000 per year) and needs to continue for life.

Because LPLD is caused by the presence of a defective gene in the patient's DNA researchers constructed a combination of a normal gene variant so that it would

act as a vector. The vector is a non-pathological virus and the gene is inserted with other elements into the genome of the virus. The vector is injected into leg-muscles of the patients and it will be incorporated into cells which is what viruses do. After incorporation in the cells, the normal mechanisms of the cell will (hopefully) express the gene and produce the enzyme.

In clinical trials it was shown that the production of normal LPL did happen and was sufficient to suppress pancreatitis and improve quality of life for these patients. The production continued for years, maybe lifelong...

Years of research led to the approval of a new gene therapy product "**Glybera**" in October 2012 by the European Commission. It was the first ever officially approved gene therapy medicinal product. After its approval the product was marketed in Europa at a cost of more than €1.000.000 per treatment, the most expensive medicine ever. But, this cost should be compared to the replacement therapy that carries a cost of 300.000 euro per year, lifelong. This again shows how delicate and difficult cost/benefit calculations are.

This high cost however was a problem and with the very small number of patients the pharmaceutical company was unable to maintain the product and in 2017 the marketing authorisation expired in the EU, a marketing authorisation is valid for only 5 years and needs to be renewed after that.

Tissue engineered medicinal product (TEMP)

A second example is an advanced therapy to repair cartilage defects in the knee. **Spherox** which are spheroids of human autologous chondrocytes to treat adult patients who suffer from symptomatic articular degeneration in the cartilage of the knee/kneecap where the size of the defect is less than 10 square cm.

The issue here is very common in young active adults, damage to the articular cartilage of the knee is not only common but it can be difficult to restore normal function.

Spherox is a tissue engineered product, cells are extensively manipulated to be useful to fulfil their task, repairing, regenerating or replacing tissue. In this case the original tissue used to make spherox is obtained from the patient himself.

A small portion of healthy cartilage tissue is removed from the patient and is sent to be transformed into a medicine for the same patient. This way there will be no problems with rejection of tissues between donor and receiver of the tissue.

This healthy tissue is then in the laboratory manipulated, chondrocytes are isolated and cultured in vitro (in a laboratory) to form 3-dimensional structures called spheroids. This suspension is then re-implanted into the knee of the patient with cartilage problems.

Like any other medicinal product ATMP's must provide a positive risk/benefit ratio in carefully executed clinical trials. These were also done for Spherox. Tests were carried out in a Phase II trial on 75 patients and a Phase III (registration) trial is ongoing. Clinical tests are progressing since 2004, in all patients a significant improvement was noted both using objective evaluation tools as well as using subjective patients reported outcomes.

As in many of these novel treatments long term outcomes are not yet available but will be further monitored over at least 5 years. Spherox received a positive opinion from the CAT committee and from the CHMP in May 2017, the European Commission granted a marketing authorisation in July 2017.

CAR-T cells

Finally, and with more details, a third example of an ATMP. This year two similar products received a positive opinion from the CAT and the CHMP and received a marketing authorisation from the European Commission for the treatment of Acute Lymphoblastic Leucemia (ALL) in children and or adult patients with diffuse large B-cell lymphoma (DLBCL) both are blood cancers. Both diseases are cancers of the B-cells which are a kind of white blood cells that play a major role in our immune system, these cells produce the antibodies to fight infection.

The two medicines are "Kymriah" and "Yescarta" and were approved at the same time this year. They both use a similar technology, CAR-T cells. What are CAR-T cells? Both ATMP's are permitted only when other treatment options failed, as a last resort for treatment.

The basis of the treatment is that B-cells have at their cellular membrane specific proteins sticking out. These antigens have functions in the normal physiology and there are many at the surface of any cell, if we would enlarge a cell it would look like it is overgrown with trees and shrubs, but different kinds of trees and shrubs that can be identified.

On B cells one of these antigens is known as the CD-19 antigen and this antigen is quite uniquely only present on B cells. This means that if you find a cell with a CD-19 antigen at its surface you can be quite sure it is a B cell.

Since ALL and DLBCL are B-cell malignancies, these B-cells are all recognisable with a CD-19 antigen. The idea is to make "something" that homes in on all cells displaying CD-19 at their surface. When the "something" connects with these surface CD-19 the effect is that that it kills these CD-19 bearing cells. If you can do that you might have a treatment. And that is exactly what is done by both new medicines.

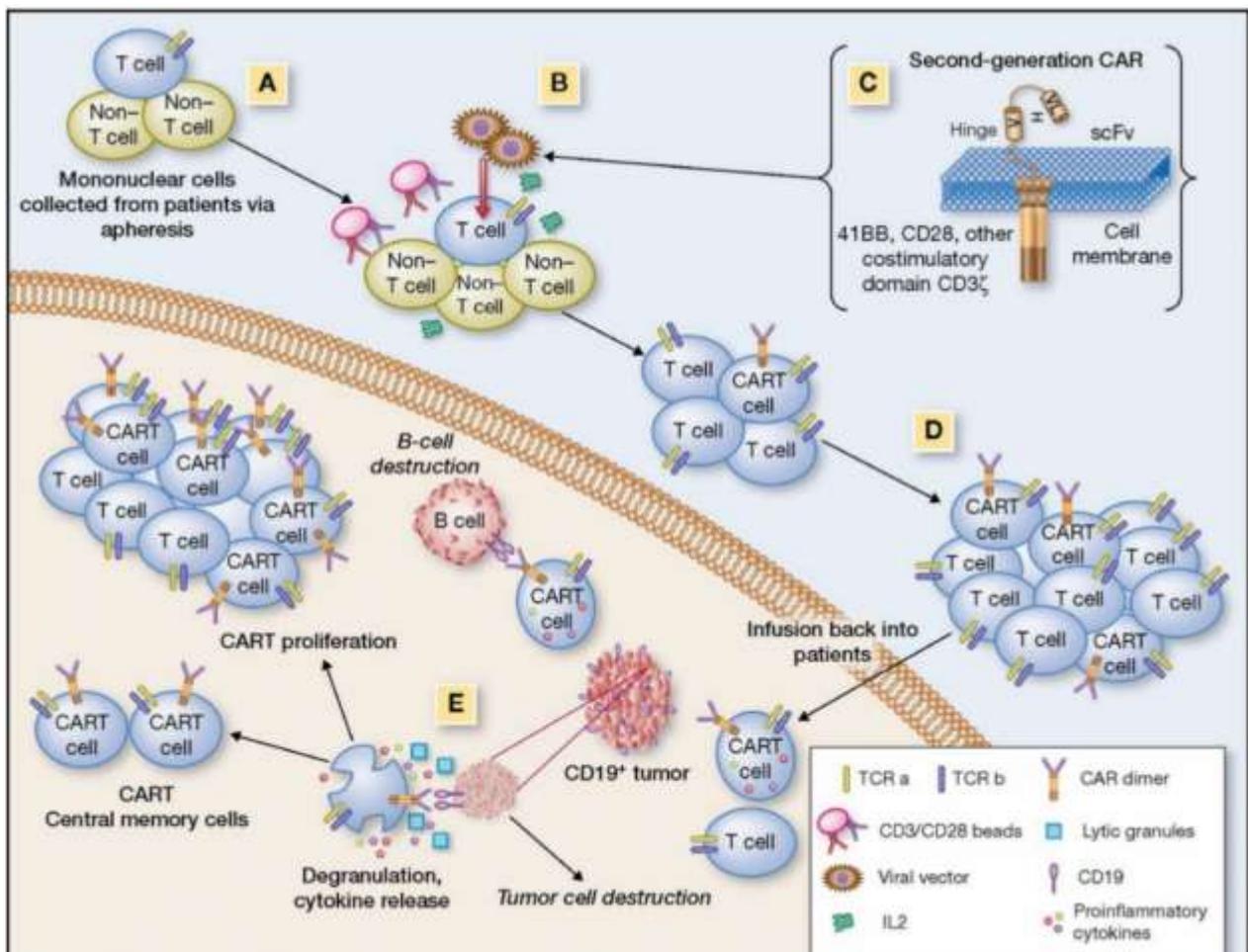
Patients are treated with their own T-cells. Which are *in vitro* modified, cultured and returned to the same patient. This means that it is an autologous treatment, no problems with compatibility between donor and receiver of the blood.

The treatment starts with harvesting a patient's own T cells (of the correct type) which are then transferred to a CAR-T cell production unit for further manipulation.

The T-cells we want to modify are what is known as "**Killer T-cells**" these cells have the property to kill cells they are hooked onto. In normal circumstances these T-cells recognize other cells as part of the immune system through specific receptors at their surface. The recognized cell can be a cancer cell, a cell that is infected with a virus, but not commonly a "B" cell. But, we can change that.

The manipulation that we are about to realise is to populate

the cellular membrane with antibodies that recognize the CD-19 antigen. The operation must result in T-cells that express a chimeric antigen receptor (CAR). To do this the T-cells are genetically modified in the laboratory to produce this receptor that can be very large and complex. After genetically modifying the T-cells to produce the desired CAR, they are cultured to produce the large quantities useful for infusion into a patient as a treatment. The desired chimeric antigen receptor in this case is an antibody recognizing CD-19.



The figure shows schematically how this works. The process starts at the top left (A), blood is taken from the patient and a specific population of white blood cells is isolated and transferred.

In step (B) selection and purification goes one step further, only T-cells are selected and grown in the laboratory.

In step (C) the T-killer cells are genetically modified to present the desired receptor at their surface.

Step (D) shows the culture and expansion of the T-cells and of the CAR-T cells to quantities high enough to treat the patient. At this point the CAR-T cell suspension is carefully controlled in every possible aspect like the number of cells, sterility etc. If all these assays turn out to be good the CAR-T cells are transported back to the patient for infusion.

(E) shown schematically what happens after the infusion. CAR-T cells will continue to proliferate as they do naturally, they even form memory cells that can wake up later when the cancer returns. The active CAR-T cells home in on B-Cells and after making contact will emit molecules to destroy them.

This is a complex treatment that also has the possibility of serious side effects that can be lethal. The patients are already very sick and for them this is really the last resort. But, because they are very sick the time to produce the CAR-T cells which is two to four weeks including two transportation steps eventually transcontinental, could be challenging. Some patients do not live to get their cells infused back and each product is useful for one patient only.

CAR-T cell treatments are very expensive, we deal with hundreds of thousands of Euros for one treatment which is another challenge even if these diseases are rare, even very rare. But the results of these treatments have been shown by the clinical trials to be very promising.

Because these patients are in a very unfavourable condition, clinical trials are often conducted in an open label and single arm model, which means that there is no comparator arm and all parties involved are made well aware of the use of the experimental medicine. In one such trial 72% of patients showed objective response after six months and 51% even showed a complete response. We must remember that these are severely sick patients who normally would die without this treatment.

The treatment cost is very high, as is to be expected for an autologous product (using the patient's own blood or cells), but the promise (to be confirmed) is that this treatment is final – a “once-off treatment”, the patient who shows complete

remission is supposed (to be confirmed) to need no further and equally expensive treatment.

What role for patients in the CAT?

It is obvious that the four patients that represent the European patients cannot be experts in all possible diseases nor novel techniques handled by the CAT. But neither are the other members of the CAT, besides the delegates for patients and health care professionals (doctors) every member state (plus Norway and Iceland) has two delegates. All members of the CAT need to study each project again from the clinical side, quality, non-clinical aspects, it is new for everybody.

But as patients we read other things in the documents that are proposed by the submitter. We look differently at the endpoints and have our own compassionate look at medical need. Our role is important because it makes the deliberations a little more “humane” and patient-centred.

Finally, the positive opinion is voted on, it is clear that, when there is an evenly split vote, the vote of any member, including a patient, can be decisive. But, if any member disagrees in a final decision, this or these members are obliged to comment on the why in writing so that the CHMP knows exactly the reasons of those who said no.

Europa Uomo as a member of the CAT

It is a big honour for our patient organization to be nominated by the European Commission to be a member or an alternate member of any committee of the European Medicines Agency. It shows that as a group we are recognized for our collaborative position at EMA and the PCWP. And it shows that the Commission is convinced that the person supported, by Europa Uomo as a delegate to the CAT, is able to assist in the evaluation of new and innovative medicines.

Learning more on EMA

EMA has a well-constructed website where you can find information on all centrally approved medicines and its committees. The website also contains information on medicines in almost all official EU languages.

Please go to: www.ema.europa.eu

If you want to find more information on a medicine you can use the search on the home page of the EMA or, for example, you can Google: “ema apalutamide”, with this you will immediately be shown pages linking the medicine and EMA.

Thanks to our sponsors during 2018-19

