

# The french perspective: The GETUG experience

*Yohann Loriot, MD, PhD*

*GU oncology, Chair, Phase 1 department, deputy head, Villejuif, France*

Is there still a room for academic clinical research ?



# Clinical research in France (GU)

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- **GETUG**= French GU Oncology group
  - 60 centers
  - 100 active investigators
- **Unicancer**= Main sponsor for clinical trials
- Fundings:
  - Ministry of Research (PHRC grants)
  - Charities
  - Industry
- Collaboration with SOGUG, EORTC, SAKK, ICORG, etc

# Structure of GETUG

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- Multi-disciplinary group:
  - Medical oncologists
  - Radiotherapists
  - Urologists
  - Pathologists, statisticians
- Open to all (public/private practice, etc)
- President elected and steering committee for 5 years (Karim Fizazi)
- All GU cancers

# Structure of GETUG

- 1994: GETUG => Chair: Prof. Jean Pierre Droz
- 1999: Chair: Prof. Stéphane Culine
- 2010: Partnership with AFU
- 2015: Intergroup ICF-URO accredited by INCa
- 2018: Intergroup GETUG-AFU-Alliance accredited by INCa
- 02/2019: Chair : Prof. Karim Fizazi



- Steering Committee:

Chair: Prof. Karim Fizazi

## Medical Oncology



☐ Dr Gwenaëlle Gravis

☐ Dr Laurence Albiges

☐ Dr Marine Gross-Goupil

☐ Dr Antoine Thiery-Vuillemin

## Radiotherapy



☐ Prof. C. Hennequin

☐ Prof. Gilles Créhange

☐ Prof. Stéphane Supiot

☐ Prof. Olivier Chapet

## Biology



☐ Prof. Yves Allory

☐ Dr Yohann Lorient

## Urology



☐ Dr Géraldine Pignot

☐ Dr François Rozet

## Statistics



☐ Dr Aurélie Bertaud

☐ Dr Boris Campillo-Gimenez

Ex officio members: Prof. Stéphane Culine – Prof. Jean-Pierre Droz

# GETUG: clinical trials

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A total of 30 clinical studies  
sponsored by other structures  
than Unicancer R&D



GETUG  
unicancer



A total of 40 clinical studies  
sponsored by Unicancer R&D

# Collaborations with pharma companies

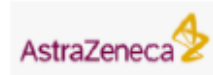
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GETUG 19



AFU-GETUG 20



GETUG 16 - GETUG 18



PEACE-6 UNFIT – PEACE-7



NIVOREN



GETUG-AFU 22



GETUG 17 & PEACE-1



PEACE-1 – CARLHA-2



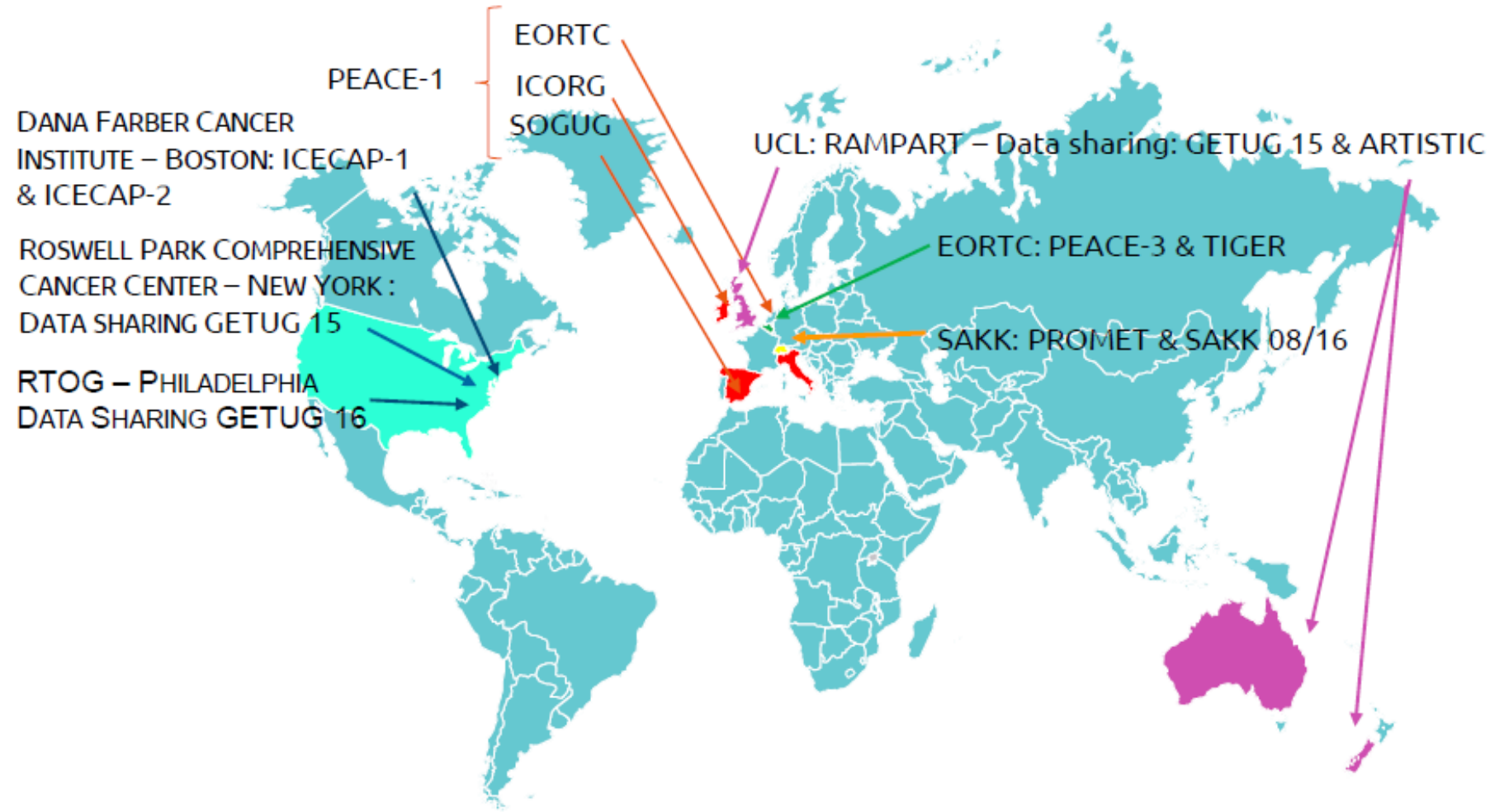
BEVABEL - ALBAN - Bladder Sparing



PEACE-1- PEACE-2

# Collaborations with international partners

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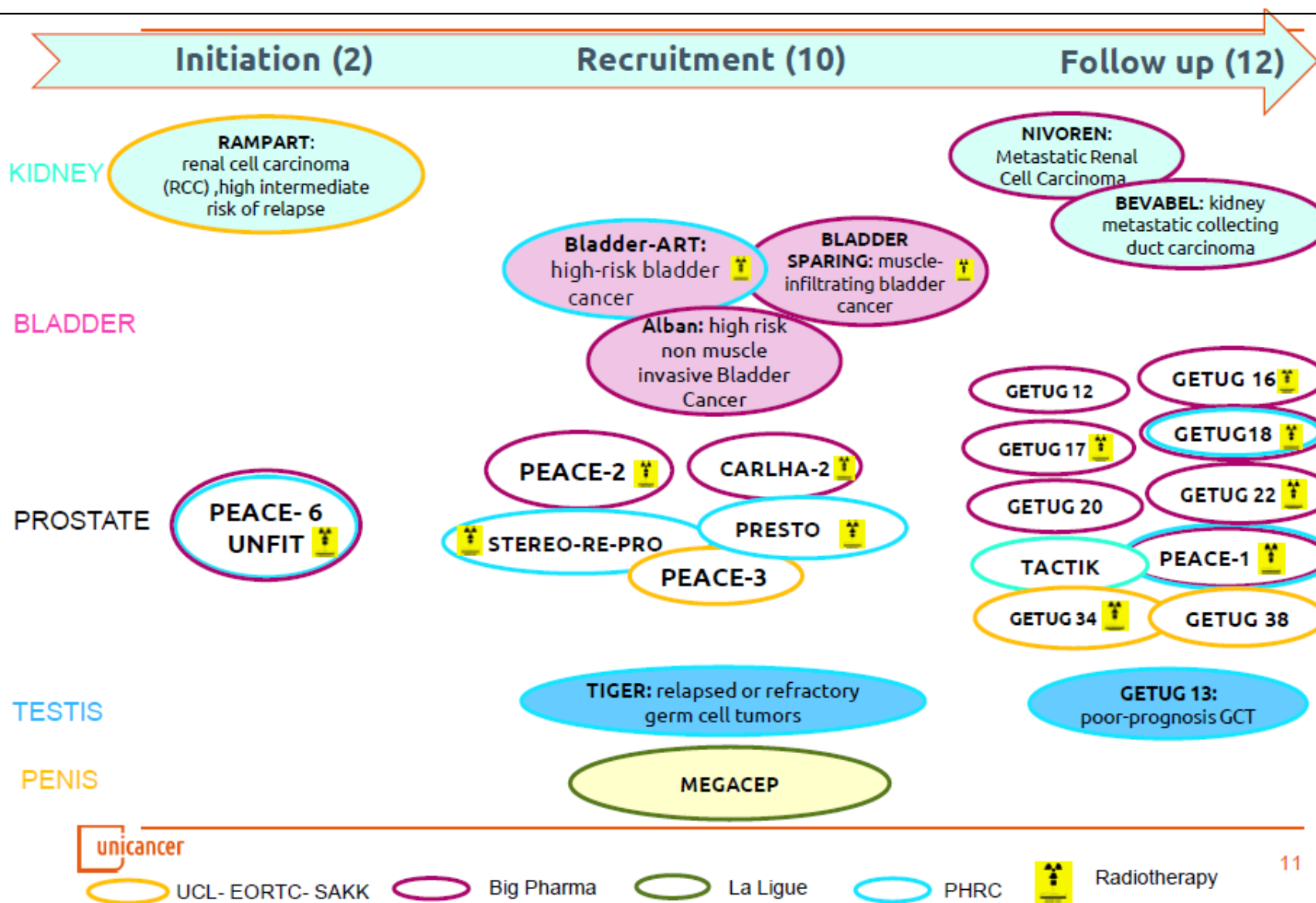
# GETUG perspective

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- Developing practice-changing phase 3 trials
- Easy to implement (pragmatic trials)
- Trials in rare tumors
- Valorizations of past clinical trials



# Recent and ongoing trials



# GETUG perspective

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- Developing practice-changing phase 3 trials
- Easy to implement (pragmatic trials)
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- Valorizations of past clinical trials

# GETUG Phase 3 trials in Prostate cancer

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| Trial name   | CaP stage                     | # pts | Main results   | Reference                |
|--------------|-------------------------------|-------|--|--------------------------|
| GETUG 01     | Localised                     | 444   | Pelvic node RXT does not increase PFS in moderate-risk CaP                   | Pommier, JCO 2007        |
| GETUG 06     | Intermediate-risk localised   | 306   | RXT 80 Gy (vs 70 Gy) provides a better 5-year biochemical outcome            | Beckendorf IJROBP 2011   |
| GETUG 12     | High-risk localised (ADT-RXT) | 413   | Docetaxel/Estramustine improves RFS  | Fizazi Lancet Oncol 2015 |
| GETUG/AFU 14 | Intermediate-risk localised   | 378   | No benefit of adding 6 months ADT to RXT 80 Gy (interim, 6 months after LPI) | Dubray 2011              |
| GETUG/AFU 15 | Newly diagnosed metastatic    | 385   | Docetaxel with ADT (vs ADT alone) improves PFS but not OS                    | Gravis Lancet Oncol 2015 |

# Ongoing GETUG phase 3 trials

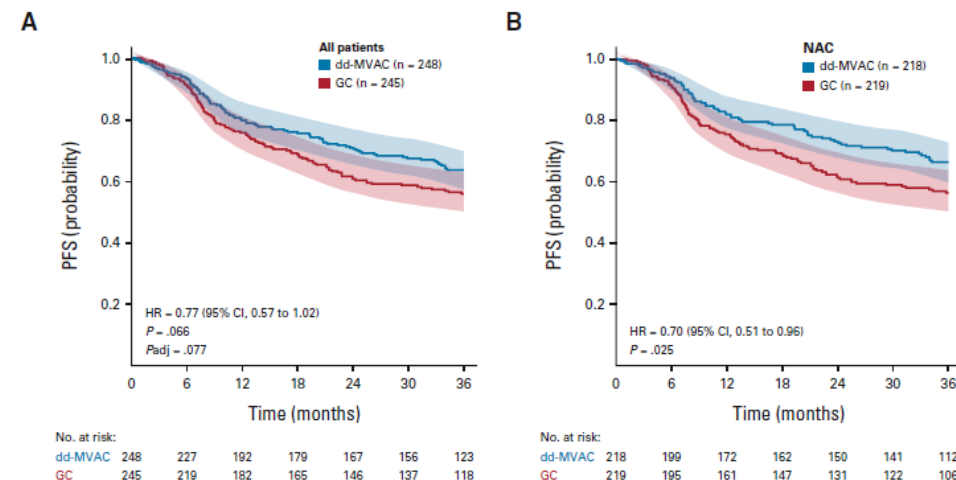
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| <b>Trial name<br/>(PI)</b>                     | <b>CaP stage</b>   | <b>Planned<br/>#pts</b> | <b>Question addressed</b>                           | <b>Accrual</b>               |
|--|--|-------------------------|---|------------------------------|
| <b>GETUG/AFU 16<br/>(Christian Carrie)</b>     | <b>Rising PSA after<br/>prostatectomy</b>                            | <b>743</b>              | <b>RXT vs RXT+ADT</b>                               | <b>Lancet oncol<br/>2019</b> |
| <b>GETUG/AFU 17<br/>(Pierre Richaud)</b>       | <b>pT3 with positive margins</b>                                     | <b>718</b>              | <b>Adjuvant vs delayed RXT<br/>+ ADT (6 months)</b> | <b>Lancet Oncol<br/>2020</b> |
| <b>GETUG/AFU 18<br/>(Christophe Hennequin)</b> | <b>High-risk localised</b>   | <b>500</b>              | <b>70 Gy vs 80 Gy RXT<br/>+ ADT (3 years)</b>       | <b>Completed</b>             |
| <b>AFU/GETUG 20<br/>(François Rozet)</b>       | <b>High-risk post-<br/>prostatectomy<br/>(pT3b or Gleason &gt;7)</b> | <b>700</b>              | <b>Adjuvant ADT<br/>vs surveillance</b>             | <b>Ongoing</b>               |

# Expanding in other tumors

## original reports Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin or Gemcitabine and Cisplatin as Perioperative Chemotherapy for Patients With Nonmetastatic Muscle-Invasive Bladder Cancer: Results of the GETUG-AFU V05 VESPER Trial

Christian Pfister, MD, PhD<sup>1,2</sup>; Gwenaëlle Gravis, MD<sup>3</sup>; Aude Fléchon, MD<sup>4</sup>; Christine Chevreau, MD<sup>5</sup>; Hakim Mahammedi, MD<sup>6</sup>; Brigitte Laguerre, MD<sup>7</sup>; Aline Guillot, MD<sup>8</sup>; Florence Joly, MD, PhD<sup>9</sup>; Michel Soulié, MD, PhD<sup>10</sup>; Yves Allory, MD, PhD<sup>11</sup>; Valentin Harter, MSc<sup>12</sup>; and Stéphane Culine, MD, PhD<sup>13</sup>; for the VESPER Trial Investigators



### Important lessons:

- 1- Example of collaboration between med oncs/uro/RXT
- 2- Frequent situation=accrual success.

A. M. L. Cormier, H. Lang, L. Guy, G. Gravis, F. Kolland, C. Linassier, E. Lechevallier, C. Beisland, M. Aitchison, S. Oudard, J.-J. Patard, C. Theodore, C. Chevreau, B. Laguerre, J. Hubert, M. Gross-Goupil, J.-C. Bernhard, L. Albiges, M.-O. Timsit, T. Lebreton, and B. Escudier

| No. at risk               | 0   | 6   | 12 | 18 | 24 | 30 | 36 | 42 | 48 |
|---------------------------|-----|-----|----|----|----|----|----|----|----|
| Nephrectomy+<br>sunitinib | 226 | 110 | 61 | 40 | 19 | 11 | 4  | 1  | 0  |
| Sunitinib alone           | 224 | 128 | 76 | 44 | 26 | 8  | 3  | 1  | 0  |

# GETUG perspective

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- Develoopping practice-changing phase 3 trials
- Easy to implement (pragmatic trials)
- Trials in rare tumors
- Valorizations of past clinical trials

# Trials in rare tumors

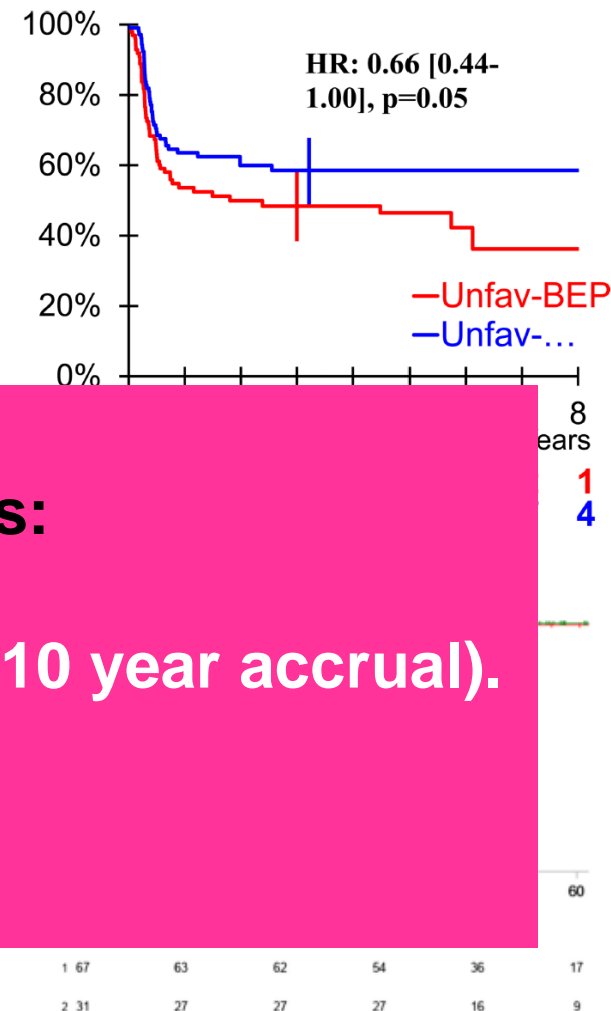
## Personalised chemotherapy based on tumour marker decline in poor-prognosis germ-cell tumours: results of the GETUG 13 phase III trial

Karim Fizazi Prof., MD<sup>1</sup>, Lance Pagliaro, MD<sup>2</sup>, Agnes Laplanche, MD<sup>3</sup>, Aude Fléchon, MD<sup>4</sup>, Josef Mardiak Prof., MD<sup>5</sup>, Lionnel Geoffrois, MD<sup>6</sup>, Pierre Kerbrat Prof., MD<sup>7</sup>, Christine Chevreau, MD<sup>8</sup>, Remy Delva, MD<sup>9</sup>, Frederic Rolland, MD<sup>10</sup>, Christine Theodore, MD<sup>11</sup>, Guilhem Roubaud, MD<sup>12</sup>, Gwenaëlle Gravis, MD<sup>13</sup>, Jean-Christophe Eymard, MD<sup>14</sup>, Jean-Pierre Malhaire, MD<sup>15</sup>, Claude Lissac Prof., MD<sup>16</sup>, Muriel Habibian<sup>17</sup>, Anne-Laure Martin<sup>17</sup>, Florence Journeau, MD<sup>18</sup>, Stephane Culine Prof., MD<sup>19</sup>

Platinum Priority – Testis Cancer  
Editorial by Peter Albers on pp. 1–7

The GETUG SEMITEP Trial  
Good-prognosis Seminoma  
Positron Emission Tomography

Yohann Loriot<sup>a,\*</sup>, Matthieu Texier<sup>a</sup>,  
Gwenaëlle Gravis<sup>f</sup>, Lionel Geoffrois<sup>g</sup>,  
Philippe Barthelemy<sup>j</sup>, Emmanuelle  
Sophie Abadie Lacourtoisie<sup>n</sup>, Christophe  
Christophe Massard<sup>r</sup>, Serena Grimaldi<sup>s</sup>, Karim Fizazi<sup>a</sup>



## Important messages:

- 1- Rare situations are challenging (10 year accrual).
- 2- Centralisation of care is key.

# GETUG perspective

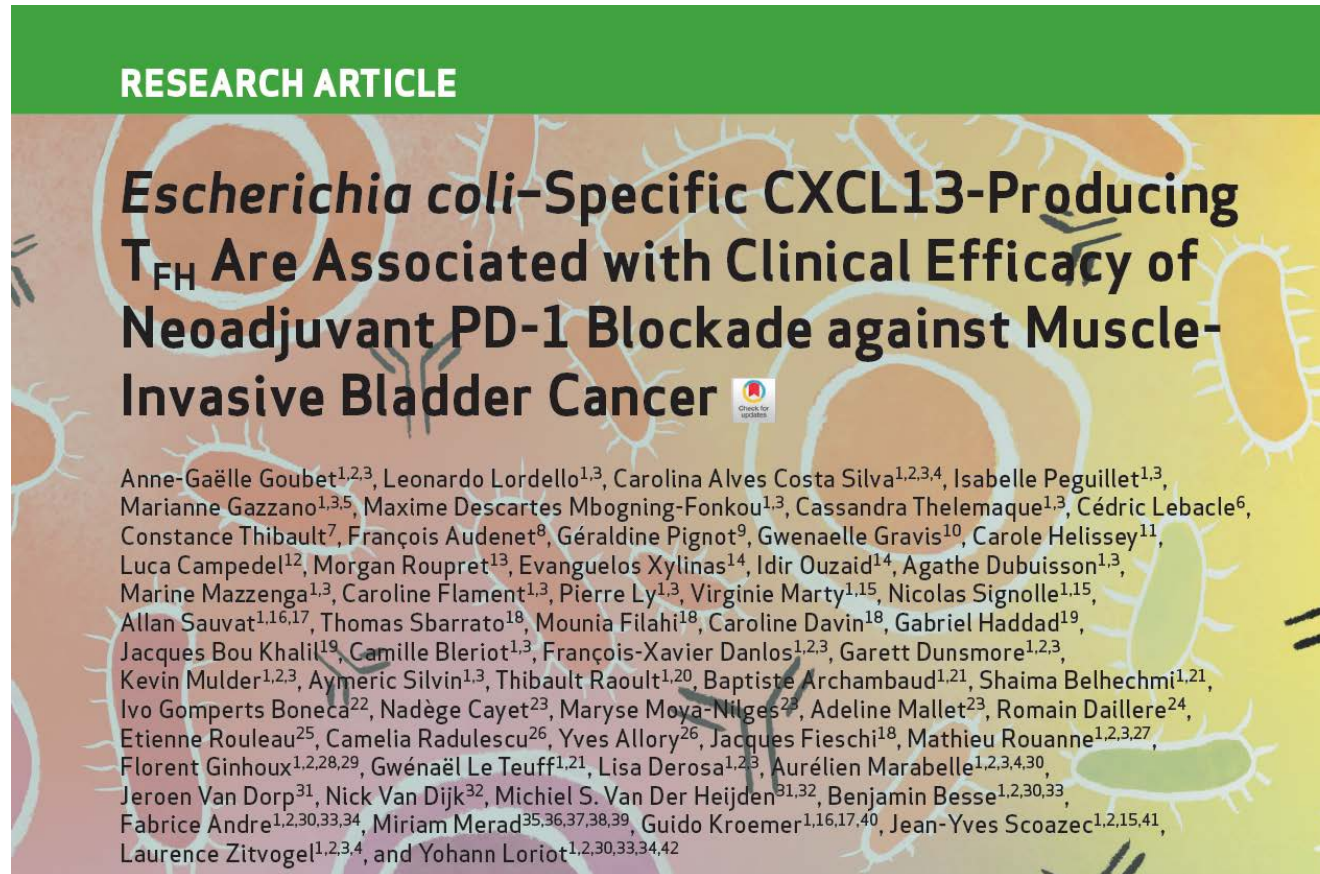
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- Developping practice-changing phase 3 trials
- Easy to implement (pragmatic trials)
- Trials in rare tumors
- To develop proof-of-concept trials (recent strategy)



# Dissecting the mechanism of action of pembrolizumab in bladder cancer

## PANDORE trials



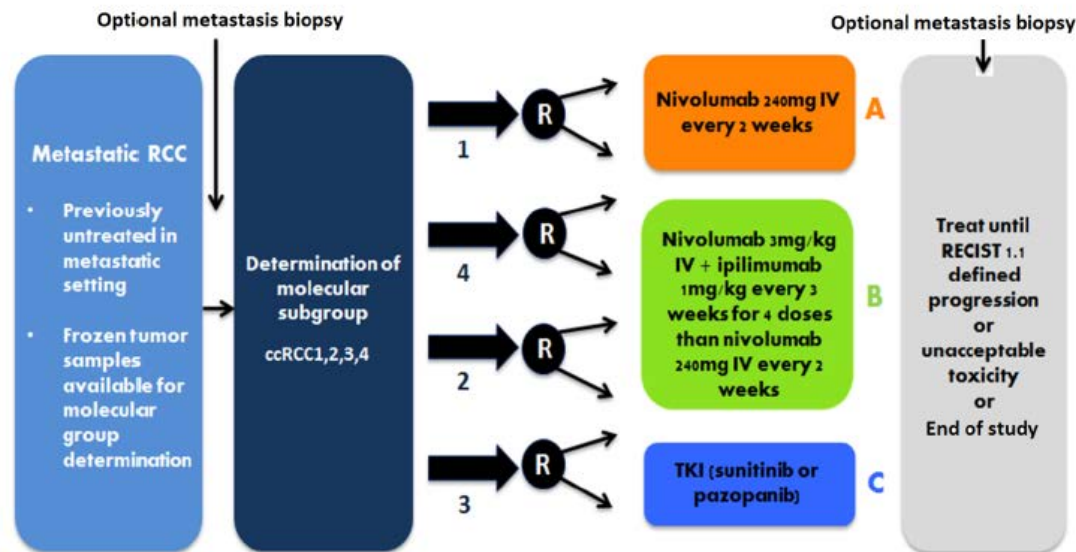
Intra-tumoral infection activates immune system and is associated with response to pembrolizumab in UBC

Goubet et al. Cancer Discovery 2022

# « Precision-medicine trials »

## Nivolumab, nivolumab–ipilimumab, and VEGFR-tyrosine kinase inhibitors as first-line treatment for metastatic clear-cell renal cell carcinoma (BIONIKK): a biomarker-driven, open-label, non-comparative, randomised, phase 2 trial

Yann-Alexandre Vano, Réza Elaidi, Mostefa Bennamoun, Christine Chevreau, Delphine Borchietti, Diane Pannier, Denis Mallet, Marine Gross-Goupil, Christophe Toumignand, Brigitte Laguerre, Philippe Barthélémy, Elodie Coquan, Gwenaëlle Gravis, Nadine Houede, Mathilde Cancel, Olivier Hurland, Philippe Beuzeboc, Laure Fournier, Arnaud Méjean, Xavier Cathelineau, Nicolas Doumerc, Philippe Paparel, Jean-Christophe Bernhard, Alexandre de la Taille, Karim Bensalah, Thibault Tricard, Thibaut Waeckel, Géraldine Pignot, Elena Braychenko, Stefano Caruso, Cheng-Ming Sun, Virginie Verkarre, Guillaume Lacroix, Marco Morello, Maxime Meylan, Antoine Bougouin, Letuan Phan, Christelle Thibault-Carpentier, Jessica Zucman-Rossi, Wolf Herman Fridman, Catherine Sautès-Fridman\*, Stéphane Oudard\*



# GETUG perspective

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- Develoopping practice-changing phase 3 trials
- Easy to implement (pragmatic trials)
- Trials in rare tumors
- Valorizations of past clinical trials

# Data sharing

## GETUG 15 Dr Gwenaëlle Gravis

THE LANCET  
Oncology



## GETUG 12 Prof. Karim Fizazi

Androgen deprivation therapy plus docetaxel and estramustine versus androgen deprivation therapy alone for high-risk localised prostate cancer (GETUG 12): a phase 3 randomised controlled trial

Karim Fizazi, Laure Faivre, François Lescunier, Remy Delva, Gwenaëlle Gravis, Frédéric Roland, Frank Priou, Jean-Marc Ferrero, Nadine Hoenes, Loïc Mourry, Christine Theodores, Jean Krakowski, Jean-François Berdel, Marjorie Bacichika, Brigitte Laquerre, Aude Ràchon, Alain Ravaud, Isabelle Cojoux-Zelik, Stéphane Oudard, Jean-Luc Laboune, Pascale Chinet-Charrat, Eric Legouffe, Jean-Léon Lagrange, Claude Linassier, Gaël Deplanque, Philippe Beuzeboc, Jean-Louis Davin, Anne-Laure Martin, Muriel Habibian, Agnès Lophanche, Stéphane Cullin

## ICECAP-1 – Dana Farber Cancer Institute

VOLUME 35 • NUMBER 27 • SEPTEMBER 20, 2017

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Metastasis-Free Survival Is a Strong Surrogate of Overall Survival in Localized Prostate Cancer

Wanfeng Xie, Meredith M. Regan, Marc Buyse, Susan Halabi, Philip W. Kantoff, Oliver Sartor, Howard Szele, Noel W. Clarke, Laurence Collette, James J. Dignam, Karim Fizazi, Wendy R. Barlow, Howard M. Sandler, Matthew R. Sydes, Bertrand Tombal, Scott G. Williams, and Christopher J. Sweeney, on behalf of the ICECAP Working Group

# Data sharing

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## GETUG-AFU 17 Dr Paul SARGOS



## ARTISTIC

Adjuvant radiotherapy versus early salvage radiotherapy plus short-term androgen deprivation therapy in men with localised prostate cancer after radical prostatectomy (GETUG-AFU 17): a randomised, phase 3 trial

*Paul Sargos, Sylvie Chabaud, Igor Latorzeff, Nicolas Magné, Ahmed Benyoucef, Stéphane Supiot, David Pasquier, Menouar Semir Abdiche, Olivier Gilliet, Pierre Graff, Cailleaud, Marlon Silva, Philippe Bergerot, Pierre Beumann, Yazid Belkacemi, David Azria, Meryem Brihoum, Michel Soulié, Pierre Richaud*

Lancet Oncol. 2020 Oct;21(10):1341-1352

Adjuvant or early salvage radiotherapy for the treatment of localised and locally advanced prostate cancer: a prospectively planned systematic review and meta-analysis of aggregate data

*Claire L Vale, David Fisher, Andrew Kneebone, Christopher Parker, Maria Pearse, Pierre Richaud, Paul Sargos, Matthew R Sydes, Christopher Brawley, Meryem Brihoum, Chris Brown, Sylvie Chabaud, Adrien Coit, Silvia Forcat, Coral Fraser-Browne, Igor Latorzeff, Mahesh K B Parmar, Jayne F Tierney, for the ARTISTIC Meta-analysis Group*

Lancet. 2020 Oct 31;396(10260):1422-1431.

# Data sharing

## GETUG 15 Dr Gwenaëlle Gravis

THE LANCET  
Oncology



UCL

To be published

ROSWELL PARK COMPREHENSIVE CANCER CENTER

To be published

## GETUG-AFU 16 Dr Christian CARRIE



RTOG

To be published

Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial

Christian Carrie, Ali Habbani, Gery de Laroché, Pierre Richaud, Stéphane Guérif, Igor Latorzeff, Stéphane Supiot, Mathieu Basset, Jean-Léon Lagrange, Véronique Bedekendorf, François Lesauvage, Bernard Dubray, Jean-Philippe Wagner, Tan Dat N' Guyen, Jean-Philippe Suchaut, Gilles Cléhange, Nicolas Barbier, Muriel Habibian, Céline Ferlay, Philippe Fourmeret, Alain Ruffion, Sophie Dussart

Lancet Oncol. 2019 Dec 20(12):1740-1749

GETUG:

**What worked/ What's working**

# What worked/ What's working

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- Accrual
- Collaboration between urologist – radiation oncologists, medical oncologists
- Rare tumors
- Trials in all stages of disease (late – early settings)



GETUG:

**What's not working !**

# What's not working !

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- Trials with complex process – infrastructure
- Time to implement the trial and rapid changing landscape
- Developing a trial (with a very good idea) when not all are convinced by the idea

# AFU-GETUG 20

## Study design

Objective : to evaluate the benefit of leuporelin acetate for 24 months after RP in patients with high risk of recurrence.

Patients : Post RP with high risk of micrometastases :

- **pT3b or Gleason score  $\geq 8$  or N+ ( $\leq 2$  nodes +) and R0**
- and M0
- with post op PSA < 0.1

—————→ RANDOMISATION

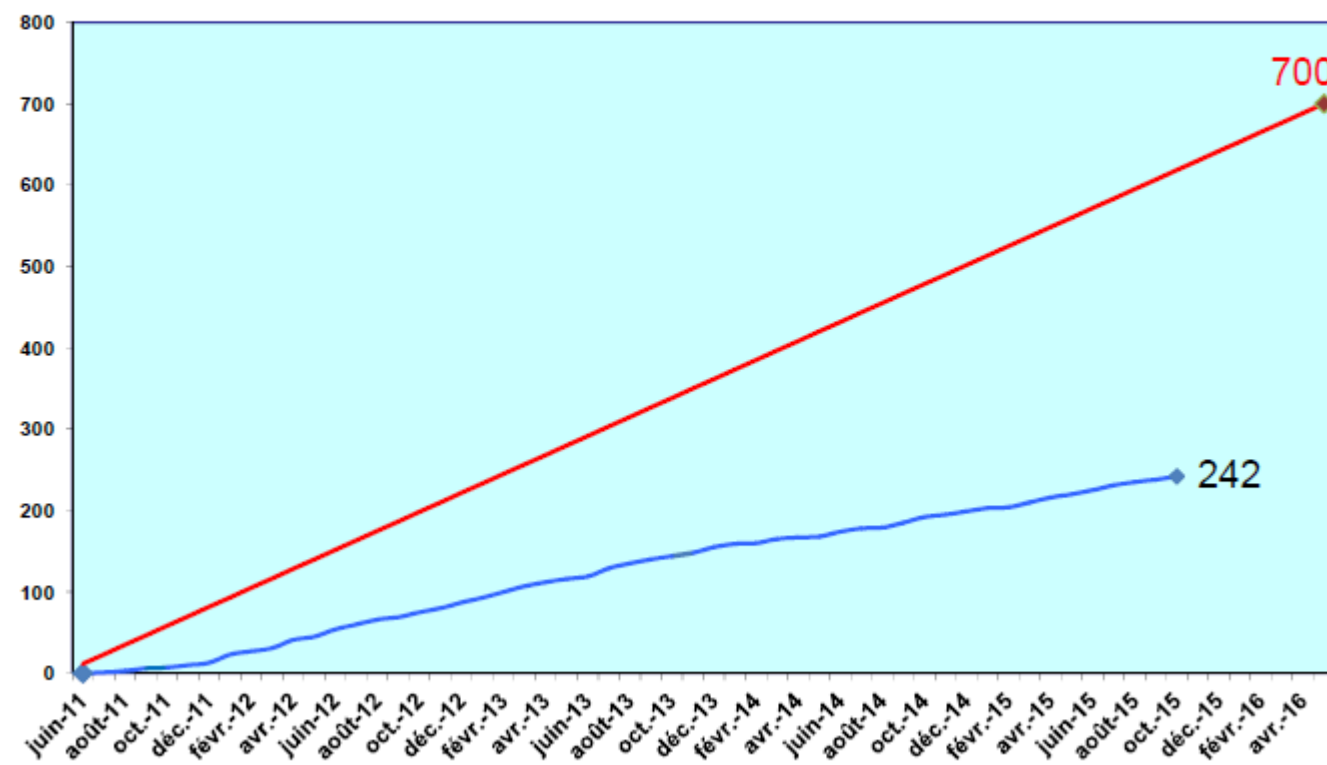
Arm A :  
Leuproréline Acétate  
- 24 months

Arm B : Surveillance

# AFU-GETUG 20



Courbe des inclusions AFU-GETUG 20 (UC-0160/1003)



# One of the most important issue of academic trials

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- Large number of patients likely needed to address important questions in the future (Phase III trials)
- National groups likely unable to make it (UK?)
- Need for a pragmatic trans-National system able to conduct such large trials

# **The PEACE program**

(Prostate Cancer Consortium in Europe)

# The PEACE program

## (Prostate Cancer Consortium in Europe)

- **Principle and aims:**
  - Academic, European program
  - Aim: conduct phase III trials for prostate cancer
  - Sponsor: any academic (Group, Hospital, University)
- **Budget:** trial by trial (academic grants, industry, charities): chair's and sponsor's responsibility
- **Publication rules:**
  - 1 chair/trial + 1 coordinator/ participating country or group
  - Best accruers also ranked by accrual
    - Ex: 1=Chair, 2=Best country coordinator, 3=Best accruer

# PEACE: Position paper

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EUROPEAN UROLOGY 67 (2015) 904–912

available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com](http://www.europeanurology.com)



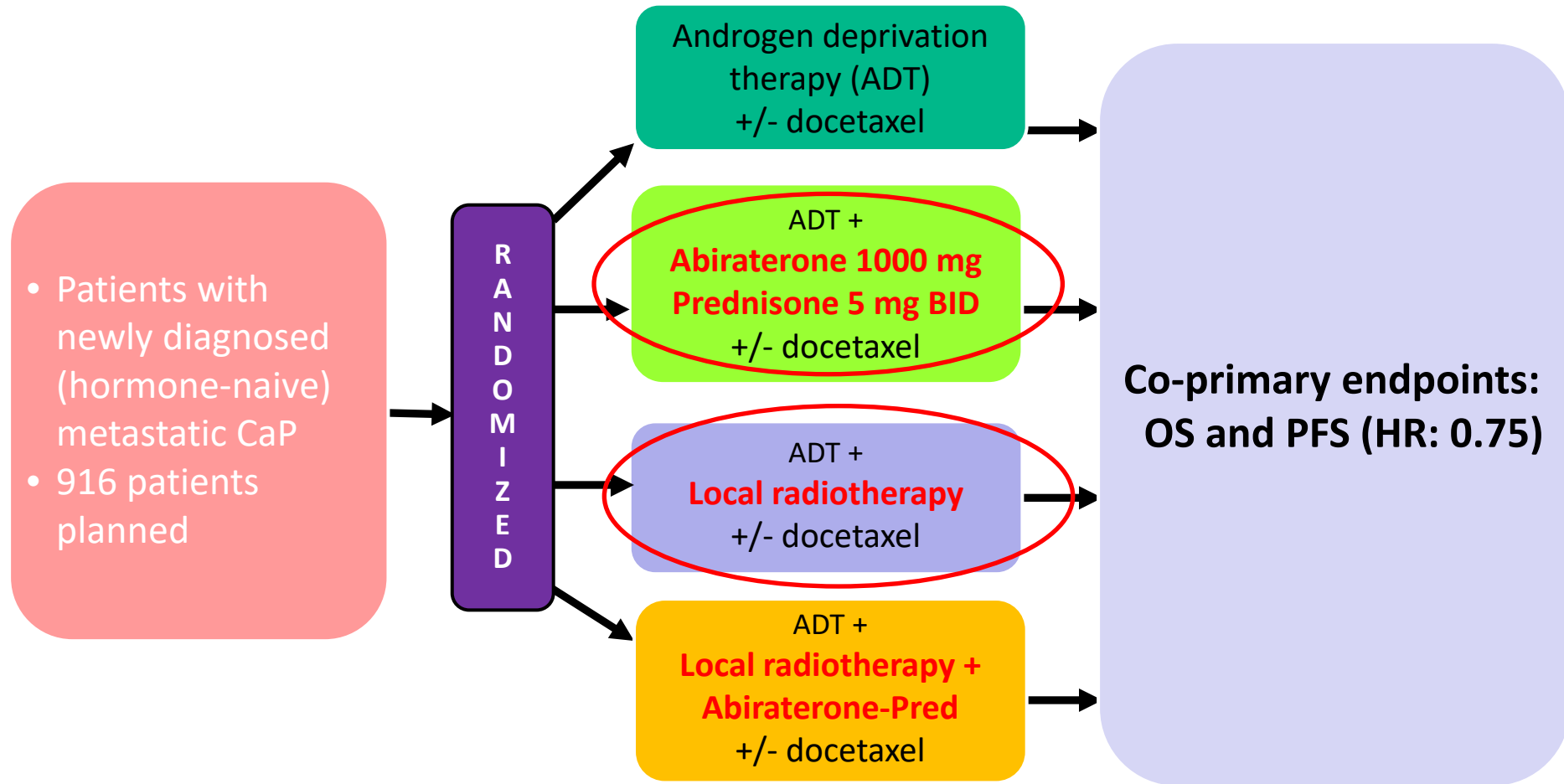
Review – Prostate Cancer

## Achievements and Perspectives in Prostate Cancer Phase 3 Trials from Genitourinary Research Groups in Europe: Introducing the Prostate Cancer Consortium in Europe

Karim Fizazi<sup>a,\*</sup>, Per-Anders Abrahamsson<sup>b</sup>, Goran Ahlgren<sup>b</sup>, Joaquim Bellmunt<sup>c</sup>, Daniel Castellano<sup>d</sup>, Stephane Culine<sup>e</sup>, Ronald de Wit<sup>f</sup>, Silke Gillessen<sup>g</sup>, Juergen E. Gschwend<sup>h</sup>, Freddie Hamdy<sup>i</sup>, Nicholas James<sup>j</sup>, Raymond McDermott<sup>k</sup>, Kurt Miller<sup>l</sup>, Thomas Wiegel<sup>m</sup>, Manfred Wirth<sup>n</sup>, Bertrand Tombal<sup>o</sup>



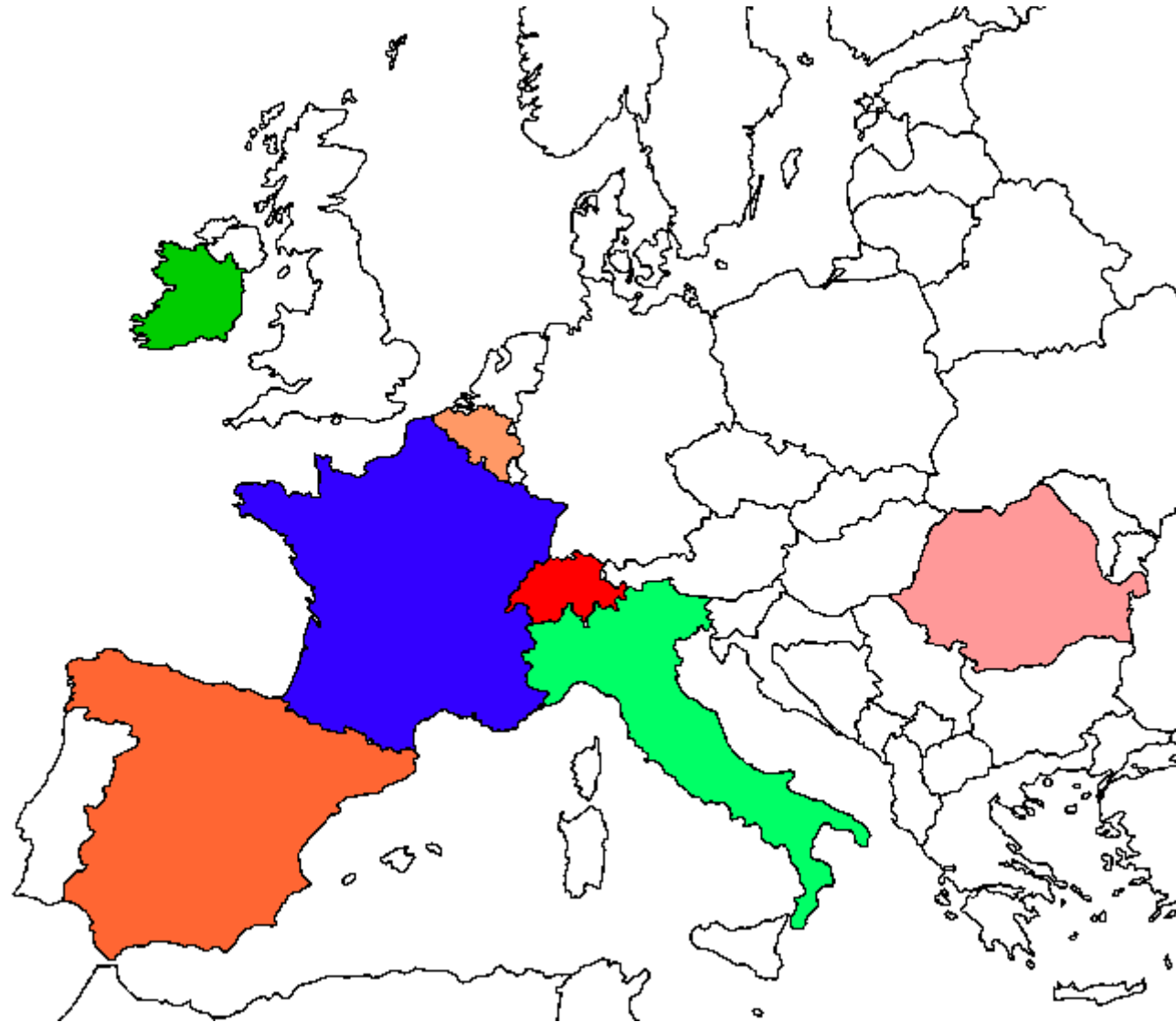
# PEACE-1: European Phase III Trial in *de novo* Metastatic Prostate Cancer (revised design)



Study sponsor: Unicancer

# PEACE-1: Participating countries

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# Collaboration makes success

THE LANCET

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## Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design

[Prof Karim Fizazi, MD](#) • [Stéphanie Foulon, MD](#) • [Prof Joan Carles, MD](#) • [Guilhem Roubaud, MD](#) •

[Prof Ray McDermott, MD](#) • [Aude Fléchon, MD](#) • et al. [Show all authors](#) • [Show footnotes](#)

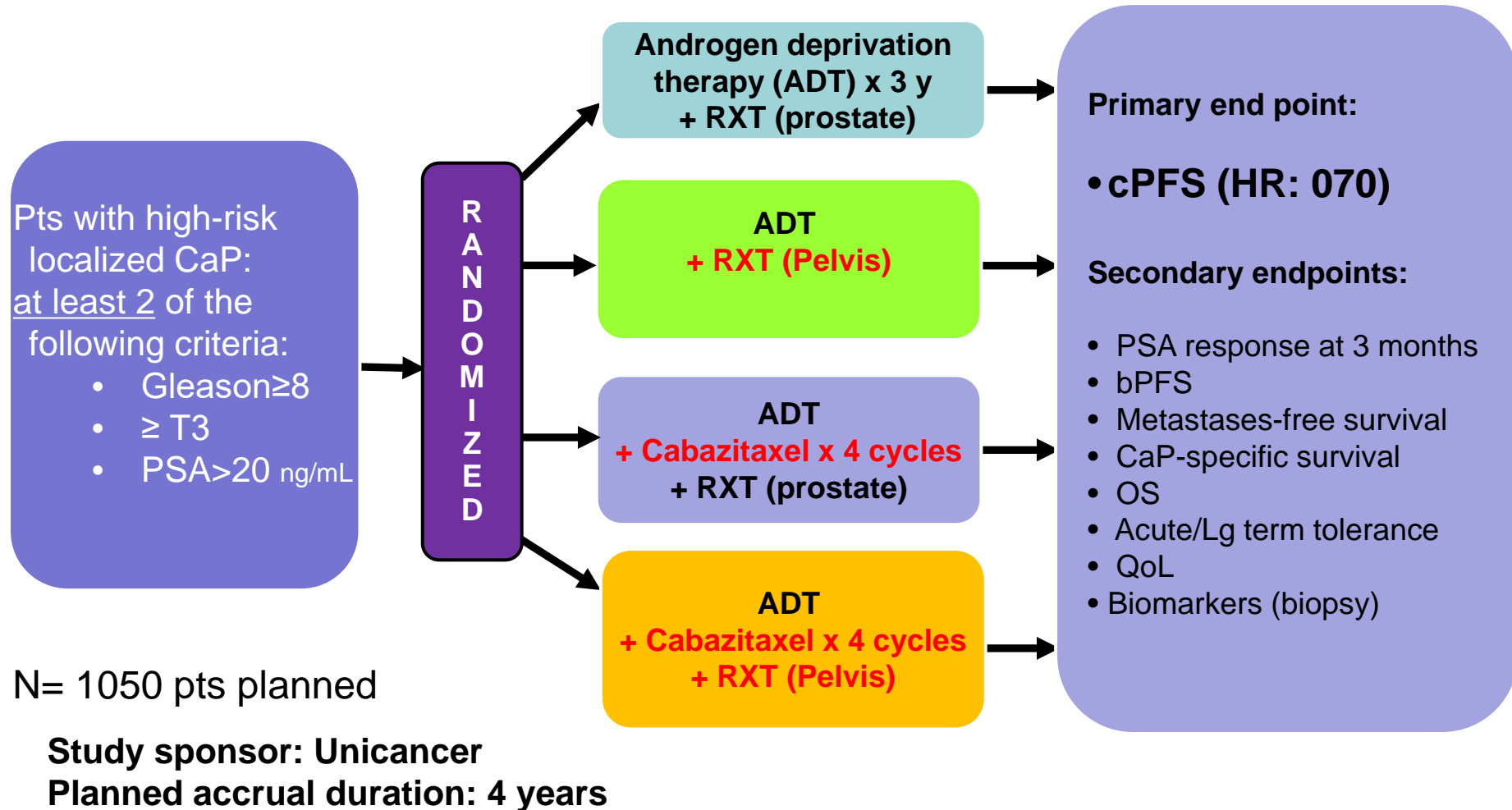
Published: April 08, 2022 • DOI: [https://doi.org/10.1016/S0140-6736\(22\)00367-1](https://doi.org/10.1016/S0140-6736(22)00367-1) •



[Check for updates](#)

PlumX Metrics

# PEACE-2: European Phase III Trial of Cabazitaxel and Pelvic irradiation in patients with high-risk localized prostate cancer



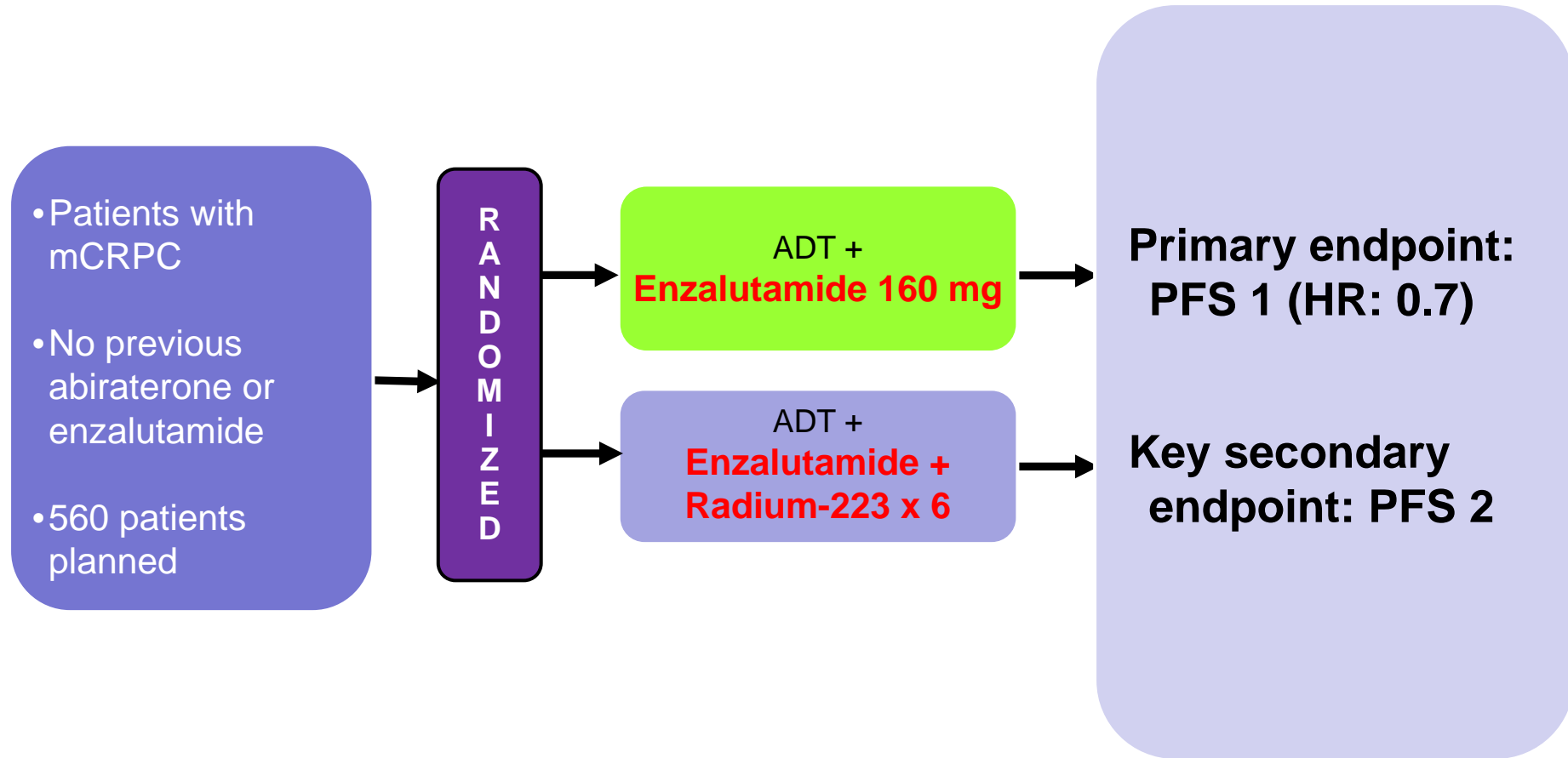
# PEACE-2: Participating countries

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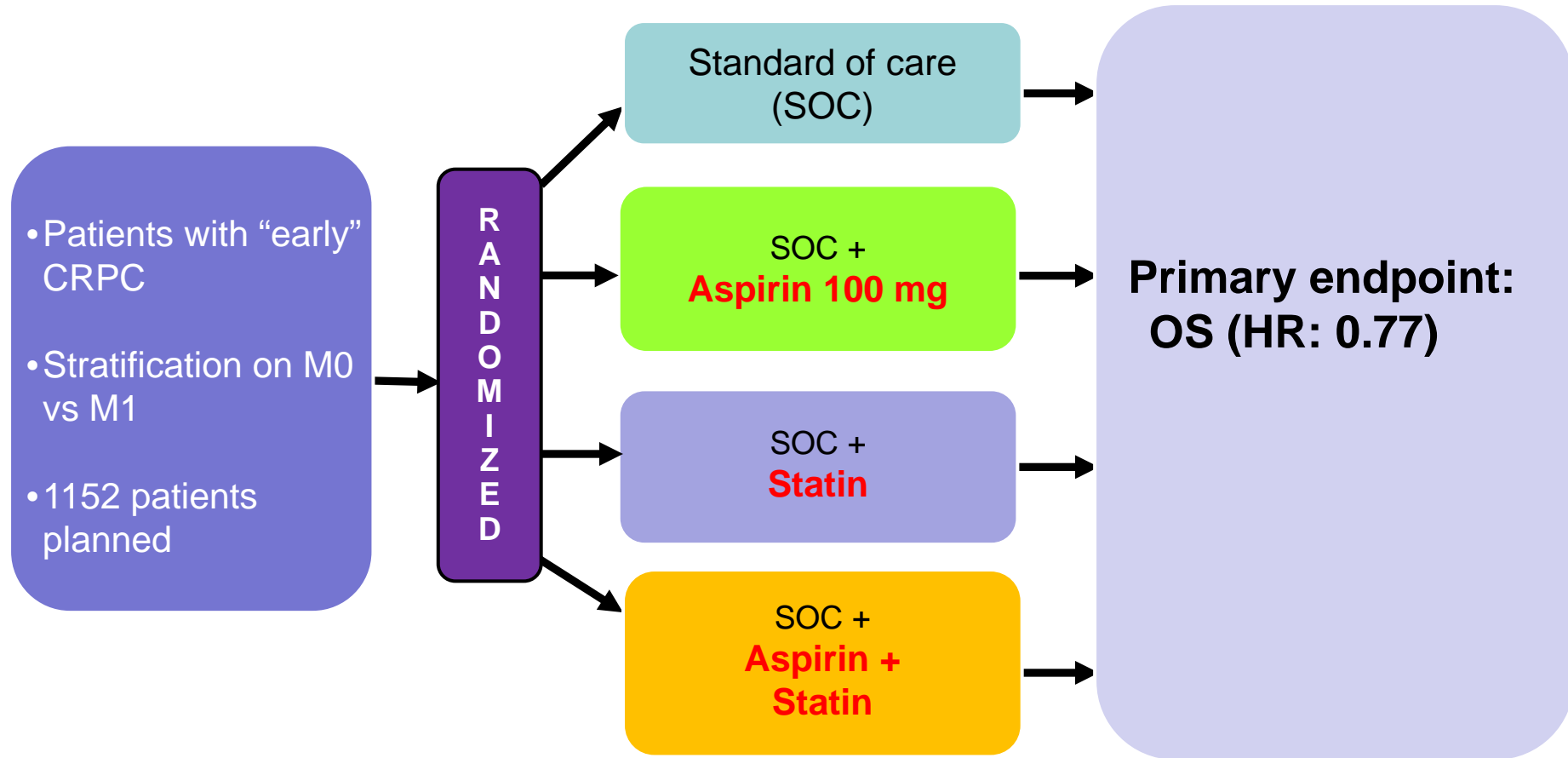
# PEACE-3: European Phase III Trial of Enzalutamide +/- Radium-223 in early mCRPC

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**Study sponsor: EORTC**  
**PI: Bertrand Tombal/ Silke Gillesen**

# PEACE-4: European Phase III Trial of Aspirin and Statin in CRPC

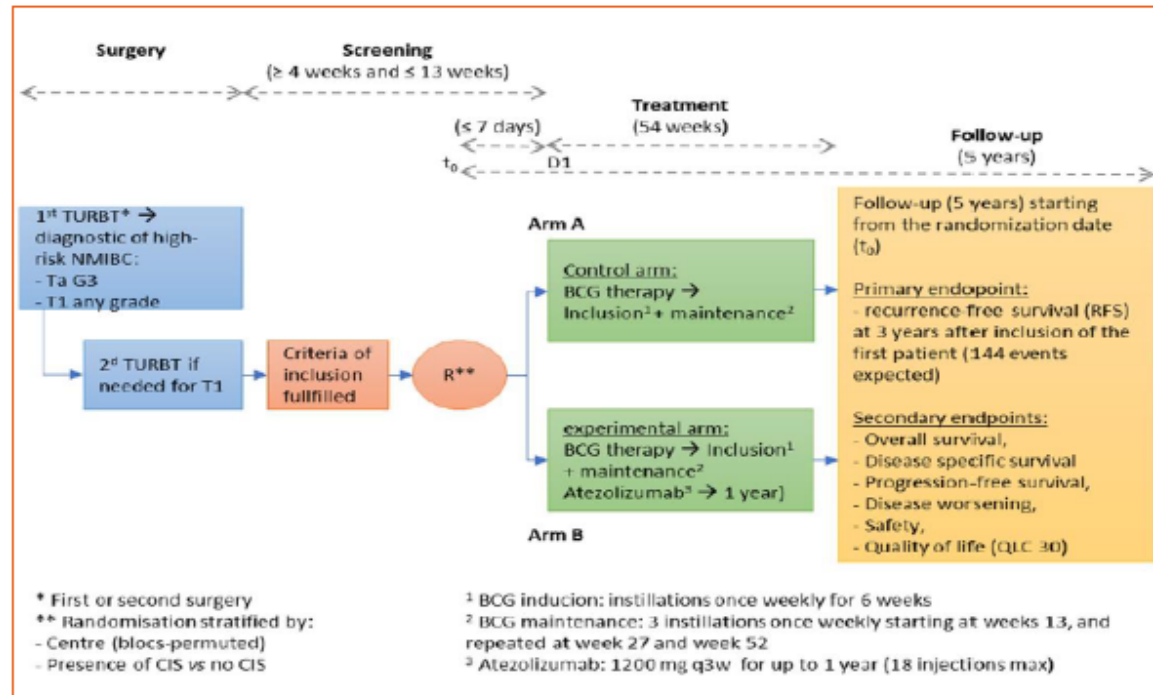


Study sponsor: Gustave Roussy

# Expanding in other tumors

## AFU-GETUG 37/ ALBAN – Prof. M. ROUPRET & Dr Y. LORIOT

An open label, randomized, phase III trial, evaluating efficacy of Atezolizumab in addition to one year BCG (Bacillus Calmette-Guerin) bladder instillation in BCG-naïve patients with high-risk non-muscle invasive Bladder cANcer

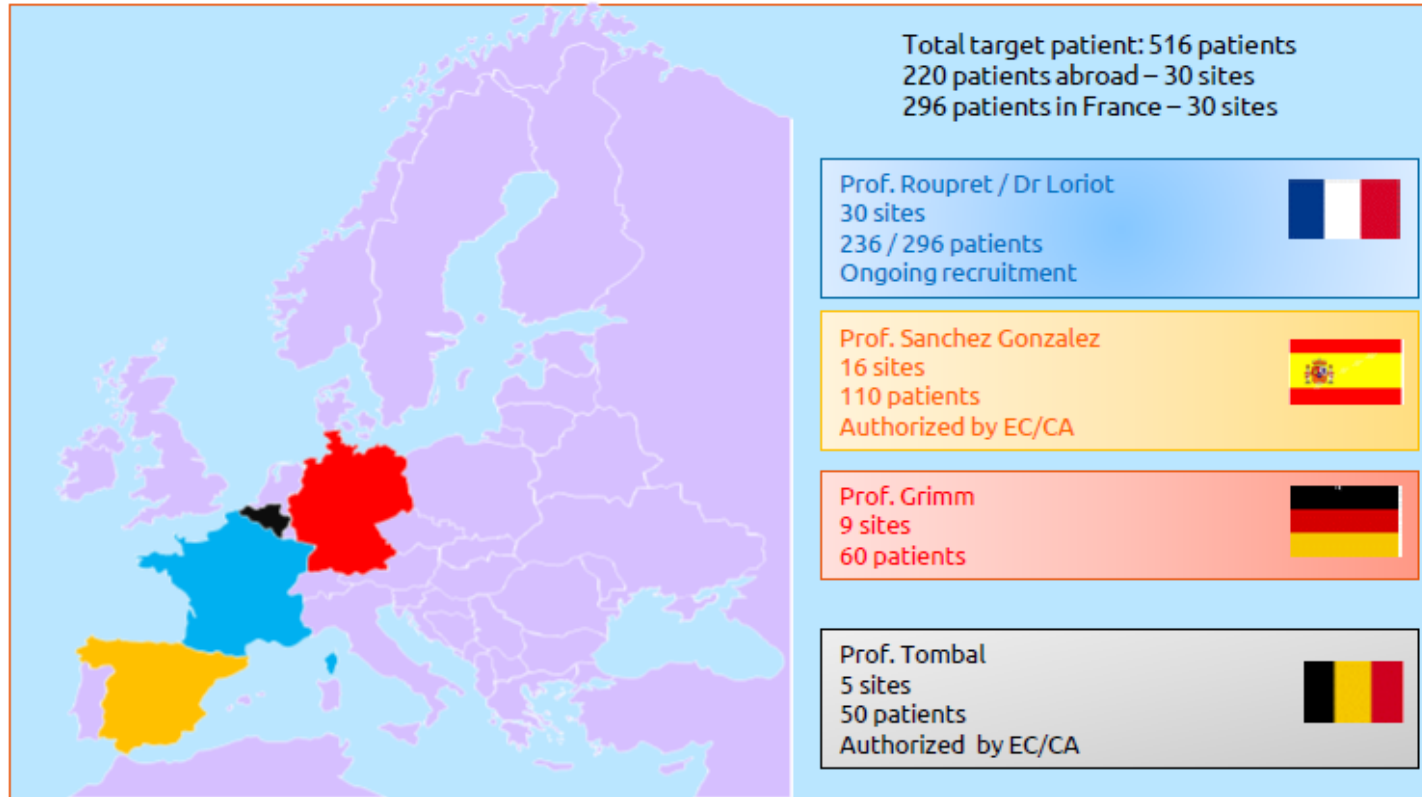


|                                |  |
|--------------------------------|--|
| Accrual period:                | 3 years and 5 months                           |
| Treatment period:              | up to 1 year                                   |
| Duration of Follow up:         | 5 years including treatment period per patient |
| Overall duration of the trial: | 8,5 years                                      |



# Expanding in other tumors

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Finally, Germany was not selected due to too many administrative hurdles

# Vision of academic clinical research

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- Main goal: to test new ideas and concepts
- How: fast, reduced cost, without too much bureaucracy.
- Drug development = mainly trials sponsored by pharmaceutical companies (which is critical for patients)
- new strategies, combinations, and exploration of different patient populations (rare tumors) = academic trials

Academic research = the way to develop the creativity, especially from young investigators

# Main problem: bureaucracy ...

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- data security -> overregulation, resulting in a reduction in research.
- Unnecessary data capture and quality control -> overwhelming role of CROs associated with increasing costs
- Data and samples sharing - > too many administrative delays and signatures and validations

Thanks to

GETUG steering committee  
K Fizazi (chair) and Soazig Nenan (Unicancer)

