EORTC
European Organisation for Research and Treatment of Cancer

Pragmatic Clinical Trials

Preliminary shared experience under the CTR

Denis Lacombe – CMF 26 February 2024

Complementary of clinical trials
The continuum drug development-access

Explanatory Clinical Trials

- Strict eligibility
- Additional procedures and processes as compared to standard
- Conducted at specific institution, organized for the complexity
- Extensive data collection and curation
- Endpoints targeting scientific knowledge and understanding of disease / intervention processes

Limited to poor external validity: the obtained estimates may not be representative of effects in the day-to-day practice. This includes both effectiveness and safety.

Pragmatic Clinical Trials

- Wide inclusion criteria
- Procedures as per standard practice
- Conducted in extended networks including community hospitals
- Limited data collection relevant to decision makers
- End-points directed to answer clinically relevant questions based on patient centric end-points

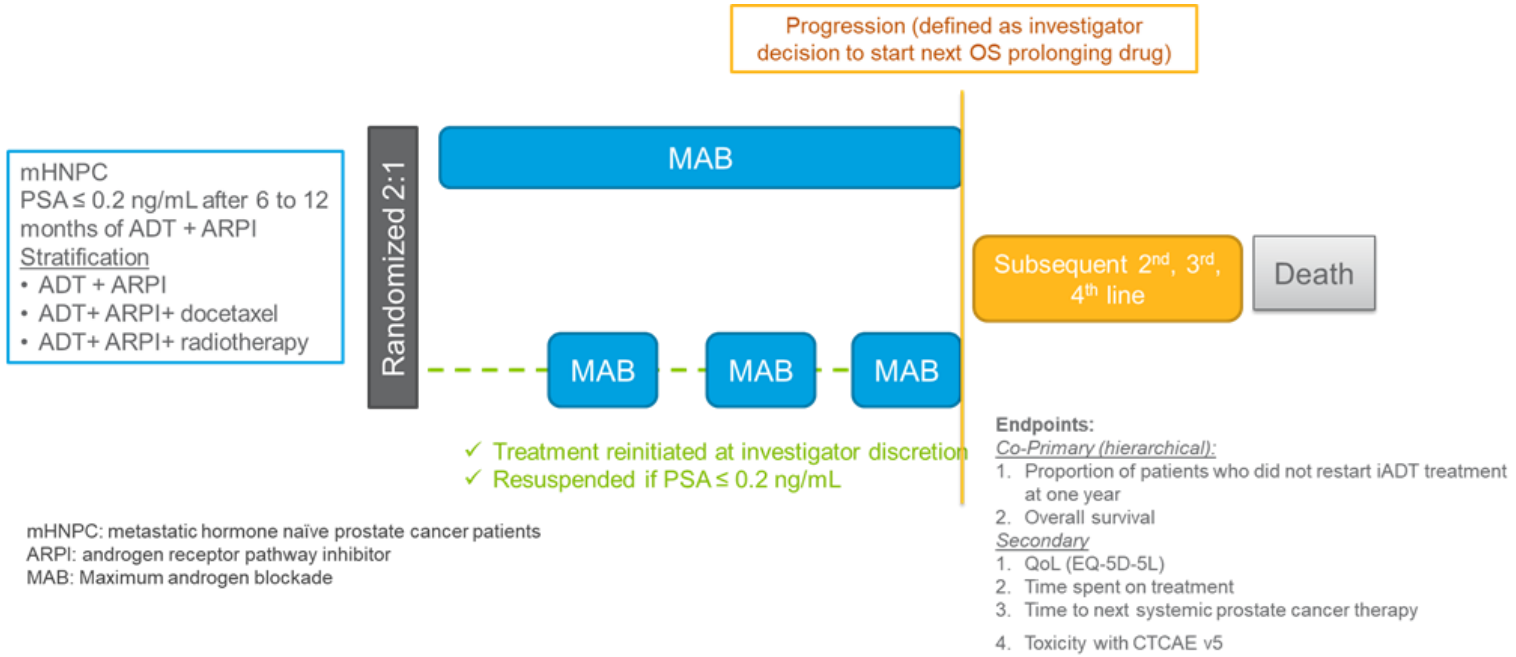
Good external validity provides information on the applicability of therapeutic interventions

Challenges of pragmatic trials

- Complex analysis
- Lack of available funding
- Lack of regulatory guidance
- Lack of specific legal framework
- Lack of experience of investigators
- Competition with explanatory trials for patient recruitment
- Ethical concerns

Ford and Norrie. *NEJM* (2016); Zuidgeest et al. *J Clin Epidemiol* (2017); Steenhuis et al. *Value Health* (2019)
Nicholls et al. *Trials* (2019)

DE-ESCALATE Intermittent Androgen Deprivation Therapy in the era of Androgen Receptor pathway inhibitors; a phase 3 pragmatic randomized trial (EORTC 2238-GUCC)



- Metastatic prostate cancer patients have been agreed with the EC as a **1st treatment optimisation study**
- It involved prostate patients' organisation to discuss and agree on the clinical endpoints to use
- 2 additional successful call in glioma and retroperitoneal sarcoma are ongoing.

Set up
- 1600 patients
~ 80 sites
~ 8 countries

Tombal Bertrand — Cliniques Universitaires Saint-Luc, Brussels
Gillessen Silke — Oncology Institute of Southern Switzerland - Ospedale San Giovanni

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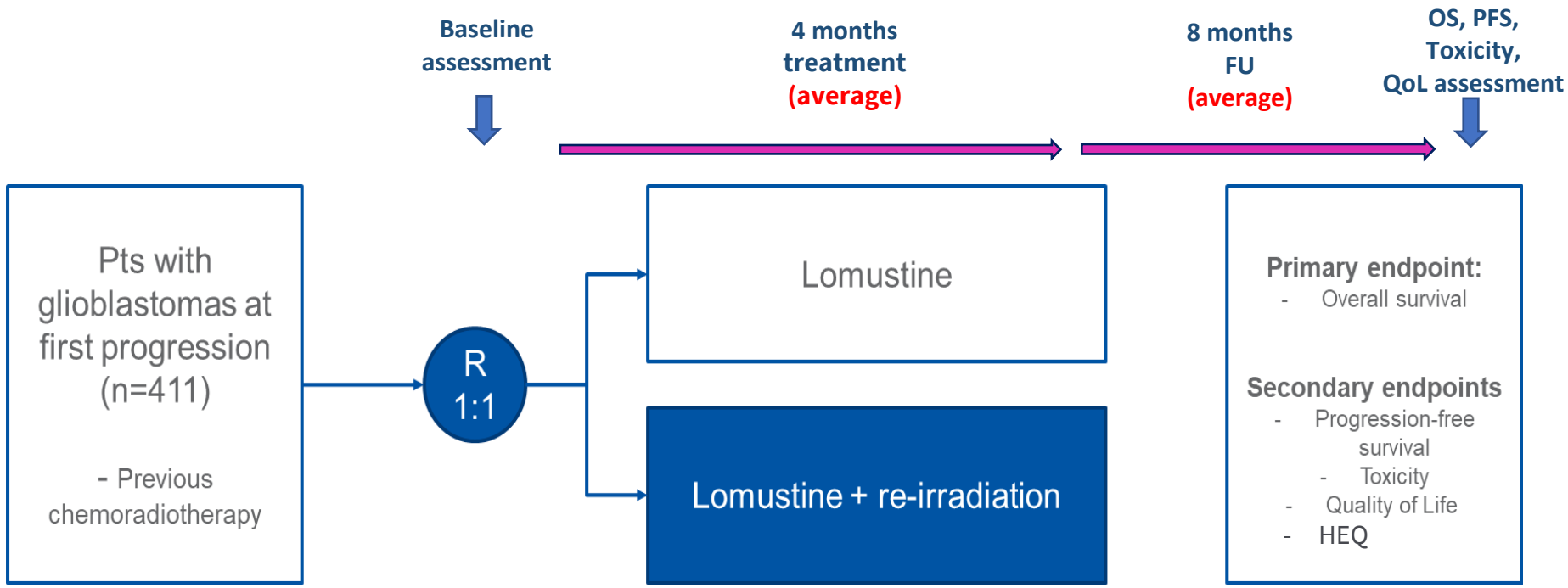
CTR challenges

- What is the std of care: treatment? Schedule?
- Definition of IMPs? Applicability to PCTs
- Low Interventional Trial status as an option!
- The concept of therapeutic strategy vs drug development

Lomustine with or without reirradiation for first recurrence of glioblastoma



Stratification factors:
- Country
- MGMT (unmeth vs meth)
- Steroids use (No,Yes)
- WHO PS (0, > 0)

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CTR challenges

- Submitted as a Low Interventional Trial
- More than 100 questions received with limited relevance for daily practice treatments and approaches
- Time, costs, resources…

Articulations for forward thinking

- Improve the understanding of PCTs
- Discuss The value and benefits of PCTs for the different stakeholders
- Understand how can PCTs help addressing the gap efficacy –effectiveness
- Identify how can PCTs subscribe to the evolving health care systems
- Alert policy makers on the need to take PCTs into account in the evolving regulatory and legal landscape
- Address the challenges to run PCTs