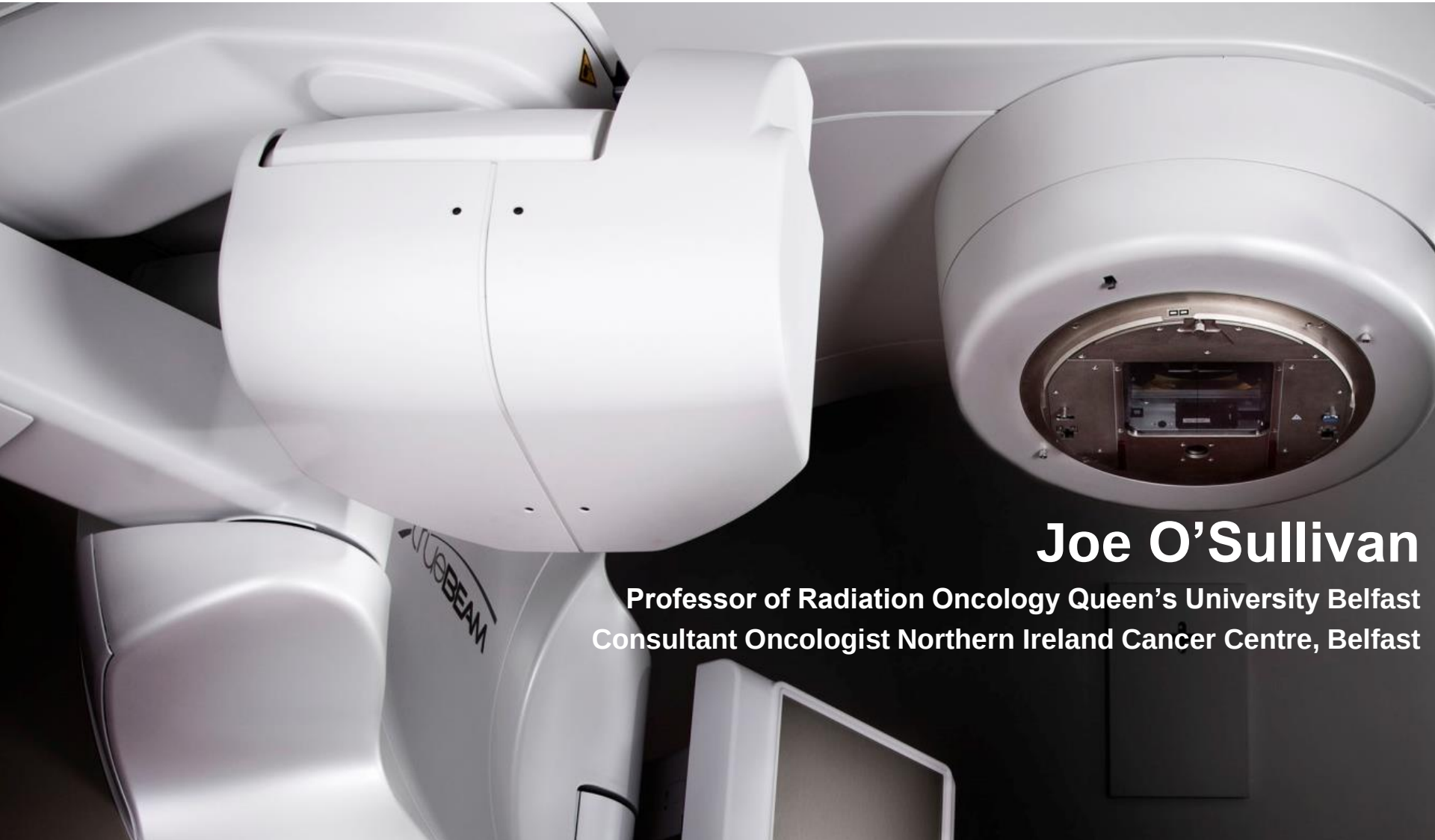
Intermediate/High Risk Prostate Cancer
How best to boost?

QUEEN'S UNIVERSITY BELFAST



Joe O'Sullivan

Professor of Radiation Oncology Queen's University Belfast

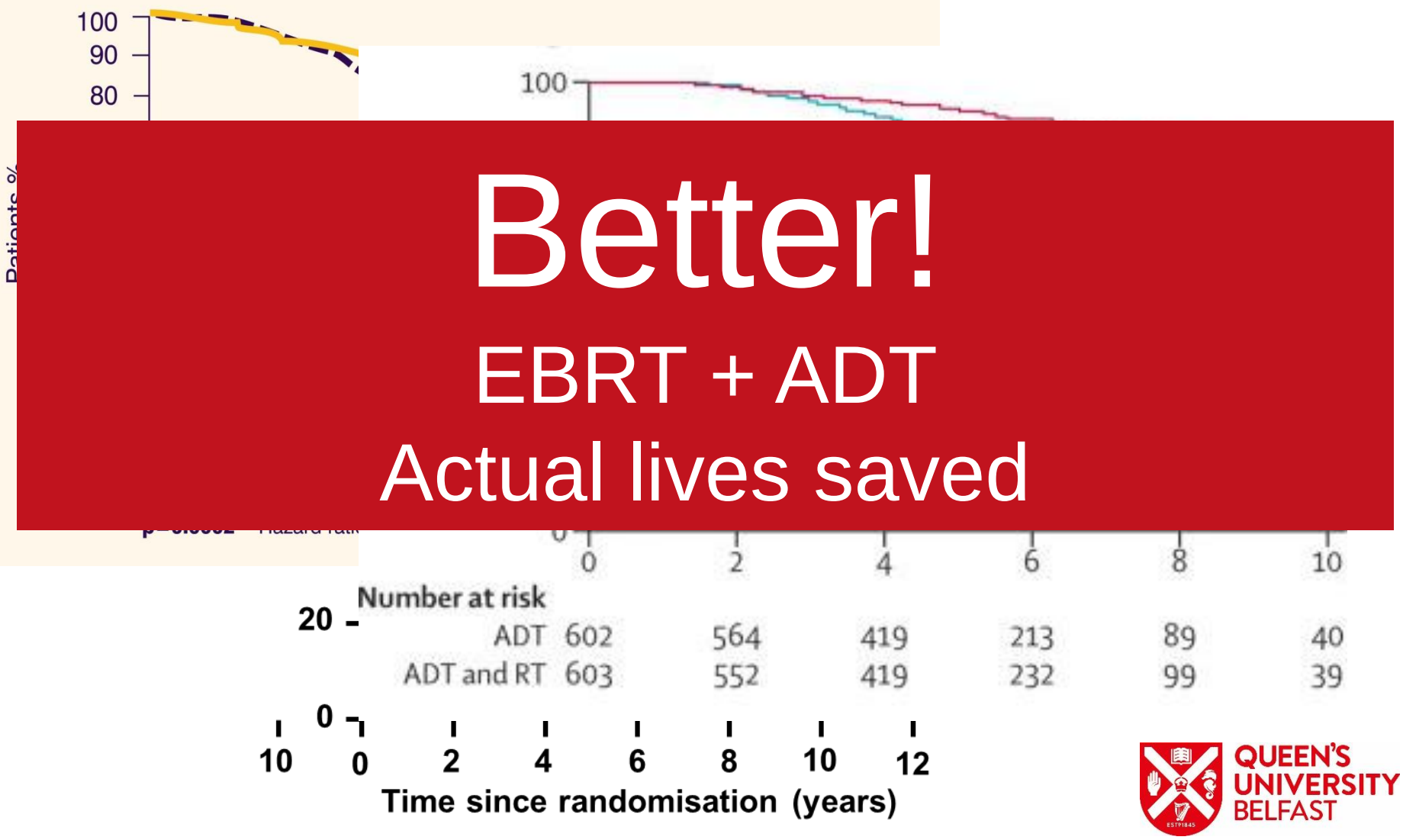
Consultant Oncologist Northern Ireland Cancer Centre, Belfast

What are we trying to achieve in treating Intermediate/high risk localised prostate cancer?

1. Cure the patient
   - Avoid mCRPC/Death from prostate cancer
   - Avoid clinically important recurrence
   - Avoid need for further therapy
2. Do no harm (or as little harm as possible)
   - As close to no toxicity as possible
3. Be Cost effective
   - Avoid need for further therapy
   - Avoid over-treatment
   - Avoid toxicity
   - Wide availability of technology/skills

QUEEN'S UNIVERSITY BELFAST

How are we doing?



Better!

EBRT + ADT

Actual lives saved

QUEEN'S UNIVERSITY BELFAST

But

- Patients with intermediate and high risk localised prostate cancer relapse
  - 10 - 40% biochemical relapse (Phoenix)
  - 10-20% clinically significant (Radiological/symptomatic)
  - 5-10% develop Metastatic disease
  - 1-7% die from prostate cancer

So… low BED, conventional, non-image guided, conformal EBRT +/- HT may not be adequate?

QUEEN'S UNIVERSITY BELFAST

My task… In Favour of EBRT

Prostate Brachytherapy Team Belfast

QUEEN'S UNIVERSITY BELFAST

The competition…

Summary of ASCENDE-RT

EBRT + LDR boost reduces PSA recurrence

(when compared to standard dose, non image-guided, EBRT using 3DCRT)

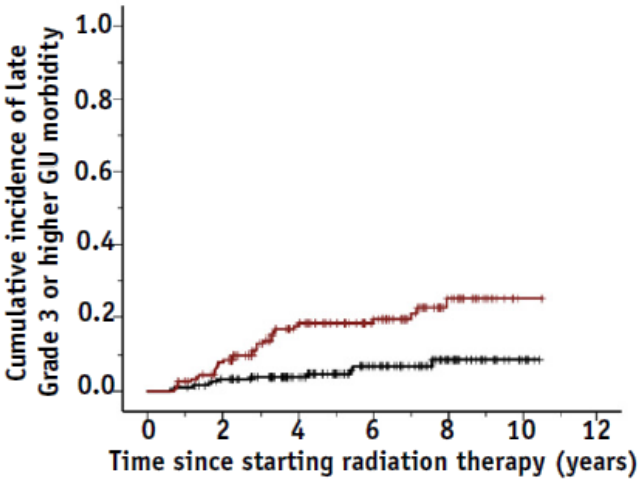
No difference in OS

No difference in MFS

Big difference in toxicity

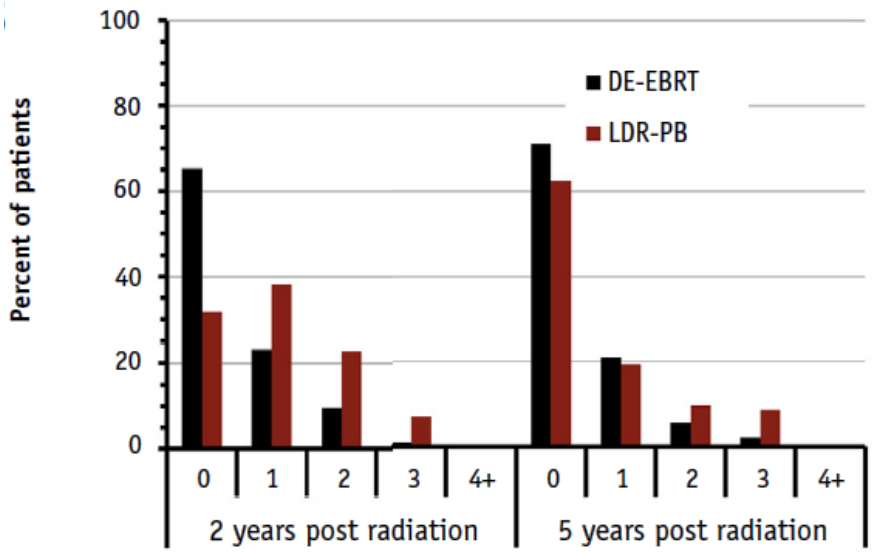
QUEEN'S UNIVERSITY BELFAST

ASCENDE-RT toxicity



Numbers at risk:

Years	0	2	4	6	8	10
DE-EBRT	195	167	125	79	41	8
LDR-PB	188	158	109	69	28	1



The prevalence of late GU morbidity by grade

QUEEN'S UNIVERSITY BELFAST

The Competition…

Summary of HDR Boost data

EBRT + HDR boost reduces PSA recurrence

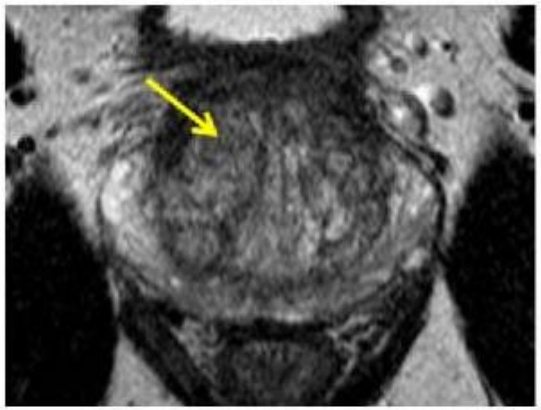
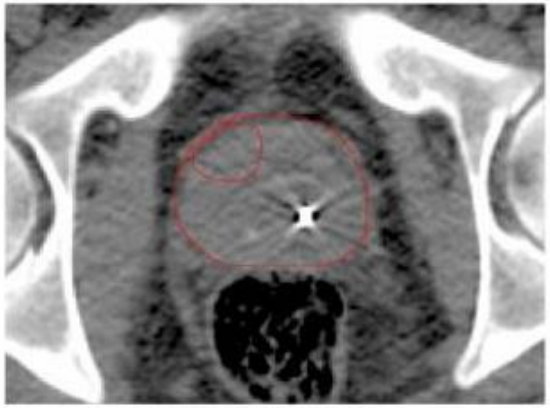
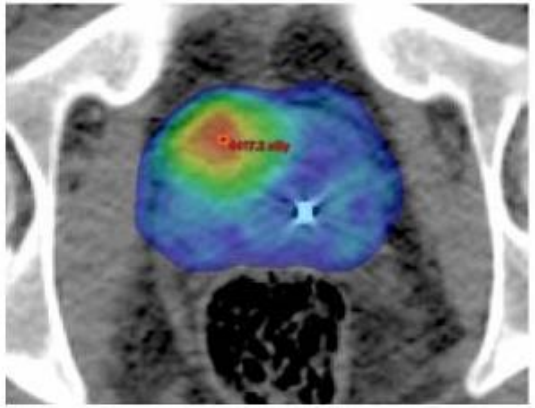
(when compared to low dose, non-image-guided EBRT using 3DCRT)

No difference in OS

No difference in MFS

QUEEN'S UNIVERSITY BELFAST

Evidence for Integrated boost, modulated IGRT?

Feasible
Phase 1 + 2 Toxicity data
Needs clinical trial evidence

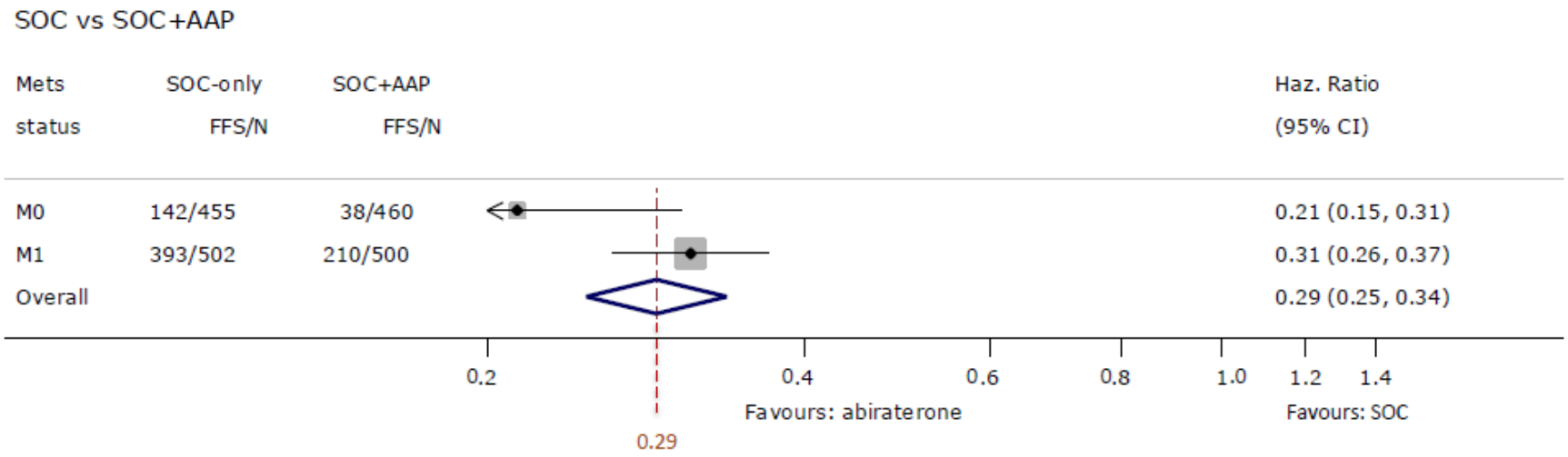
But.
Improving MRI and PET technology

And…Widely available radiation technology & expertise And..
No anaesthetic/theatre, Non-invasive, Individualised, Fast,
Adaptable, Efficient, Cost effective, And…Continuing to improve

QUEEN'S UNIVERSITY BELFAST

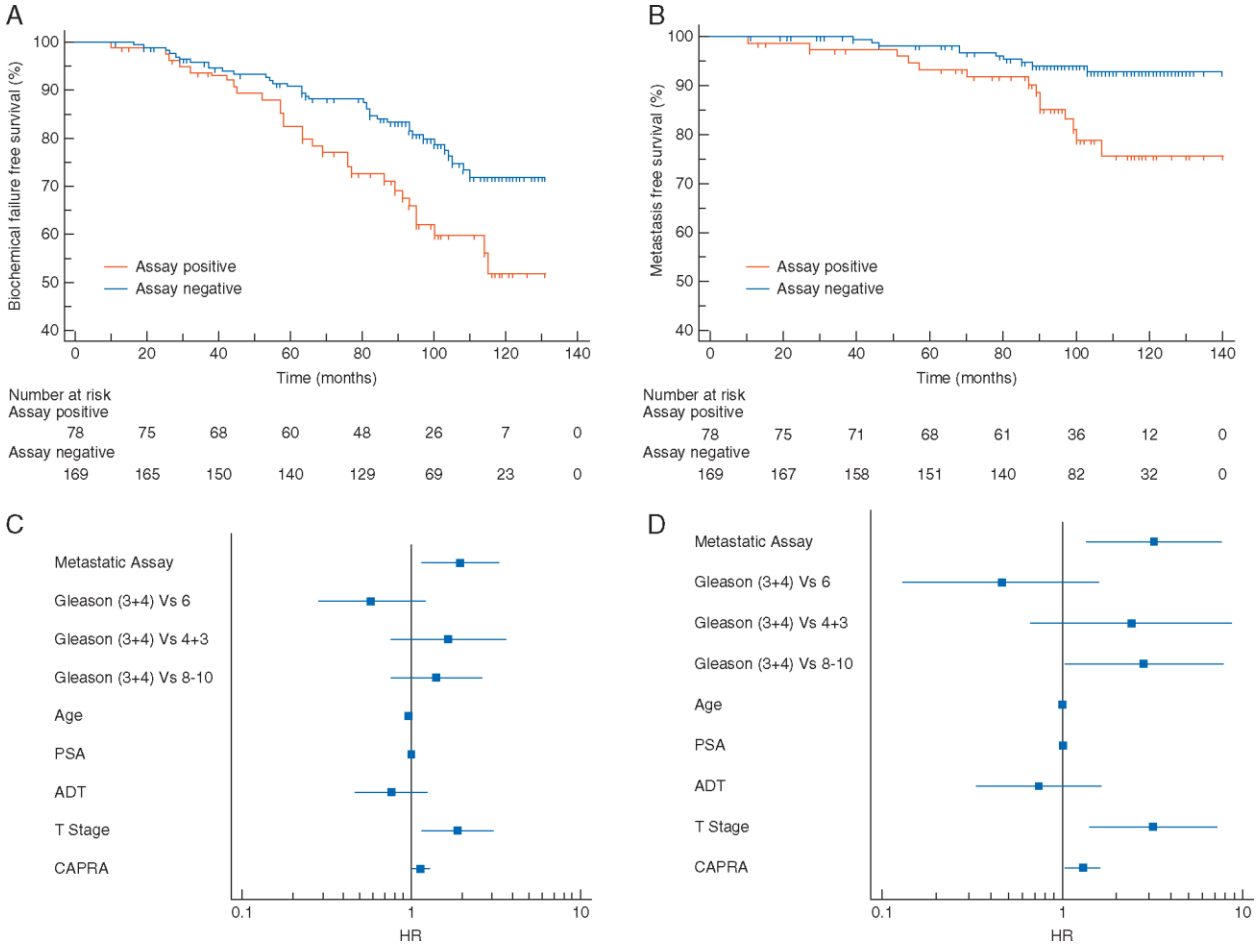
And… potential for drugs to help

STAMPEDE "abiraterone comparison"
FFS by metastatic status – pre-planned analysis



QUEEN'S UNIVERSITY BELFAST

And….biology is redefining risk categories



Jain S, Lyons CA, Walker SM, McQuaid S, Hynes SO, Mitchell DM, Pang B, Logan GE, McCavigan AM, O'Rourke D, McArt DG, McDade SS, Mills IG, Prise KM, Knight LA,, Steele CJ, Medlow PW, Berge V, Katz B, Loblaw DA, Harkin DP, James JA, O'Sullivan JM, Kennedy RD, Waugh DJ. Validation of a Metastatic Assay using biopsies to improve risk stratification in patients with prostate cancer treated with radical radiation therapy. **Ann Oncol. 2018 Jan 1;29(1):215-222. doi: 10.1093/annonc/mdx637.**

QUEEN'S UNIVERSITY BELFAST

Trials needed

	Team	P	W	D	L	PD	B	Pts
1	Ireland	5	5	0	0	78	3	26
2	Wales	5	3	0	2	36	3	15
3	Scotland	5	3	0	2	-27	1	13
4	France	5	2	0	3	14	3	11
5	England	5	2	0	3	10	2	10
6	Italy	5	0	0	5	-111	1	1

QUEEN'S UNIVERSITY BELFAST

Trials needed

- PIVOTAL Boost
- Need to prospectively collect-
  - cost effectiveness data
  - Toxicity
- Modern Imaging
- ? Genomic stratification
- We need to define meaningful end points

QUEEN'S UNIVERSITY BELFAST

External Beam Radiotherapy