HYPO-FLAME TRIAL:

5-YEAR EFFICACY AND TOXICITY OF FOCAL BOOST SBRT IN PROSTATE CANCER

Stereotactic body radiotherapy with a focal boost to the intraprostatic tumor for intermediate and high risk prostate cancer: 5-year efficacy and toxicity in the hypo-FLAME trial

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BACKGROUND

PROBLEM STATEMNT

1.4 million new cases / year

BACKGROUND ……

EBRT is Standard treatment

RATIONALE

DOSE ESCALATION

Combine biological dose escalation (SBRT)

+

physical dose escalation (focal boost).

FLAME trial

Conventional RT

+

95 Gy boost showed improved bDFS.

STUDY DESIGN

- Multi centric
- Ph II

- 100 men

(75% high-risk,

25% intermediate-risk).

- **Inclusion:**
  1. Visible mpMRI lesions,
  2. PSA <30 ng/mL,
  3. GS – 7 or more
  4. no metastases

Whole Prostate:
35 Gy in 5 weekly fractions.

Focal Boost:
Up to 50 Gy (iso-toxic, prioritized OAR constraints).

ADT:
62% received androgen deprivation

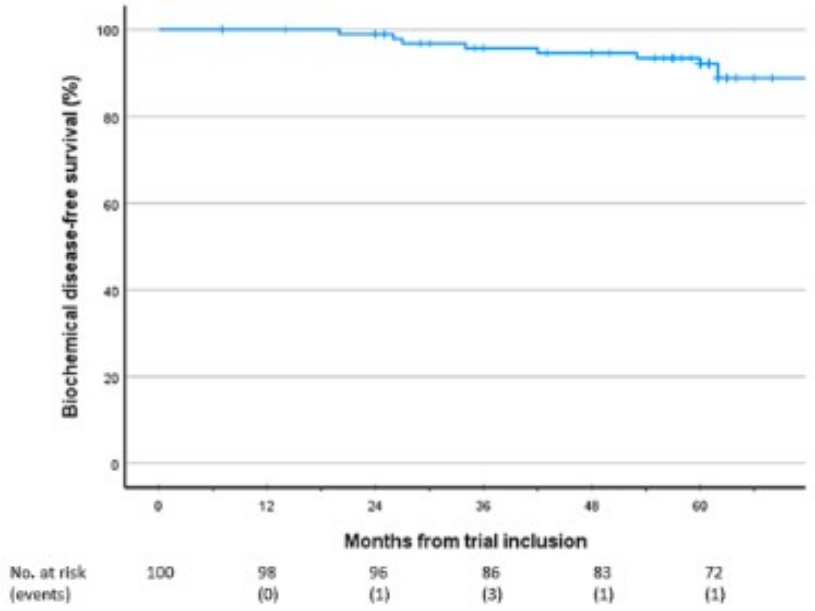
ENDPOINTS:

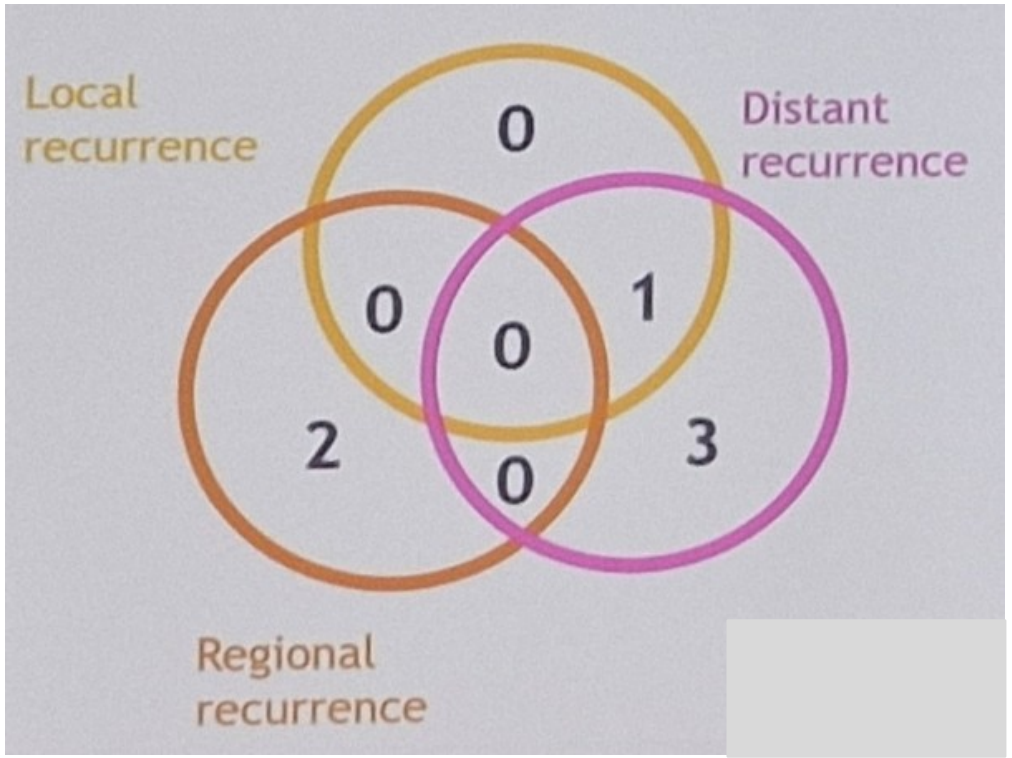
Primary:
Acute toxicity (previously published).

Secondary:
- 5-year bDFS,
- late toxicity (CTCAE v4.0),
- HRQoL (EORTC QLQ-C30/PR25).

KEY RESULT - EFFICACY

5 years bDFS = 93% (95.7% PACE B intermediate risk)



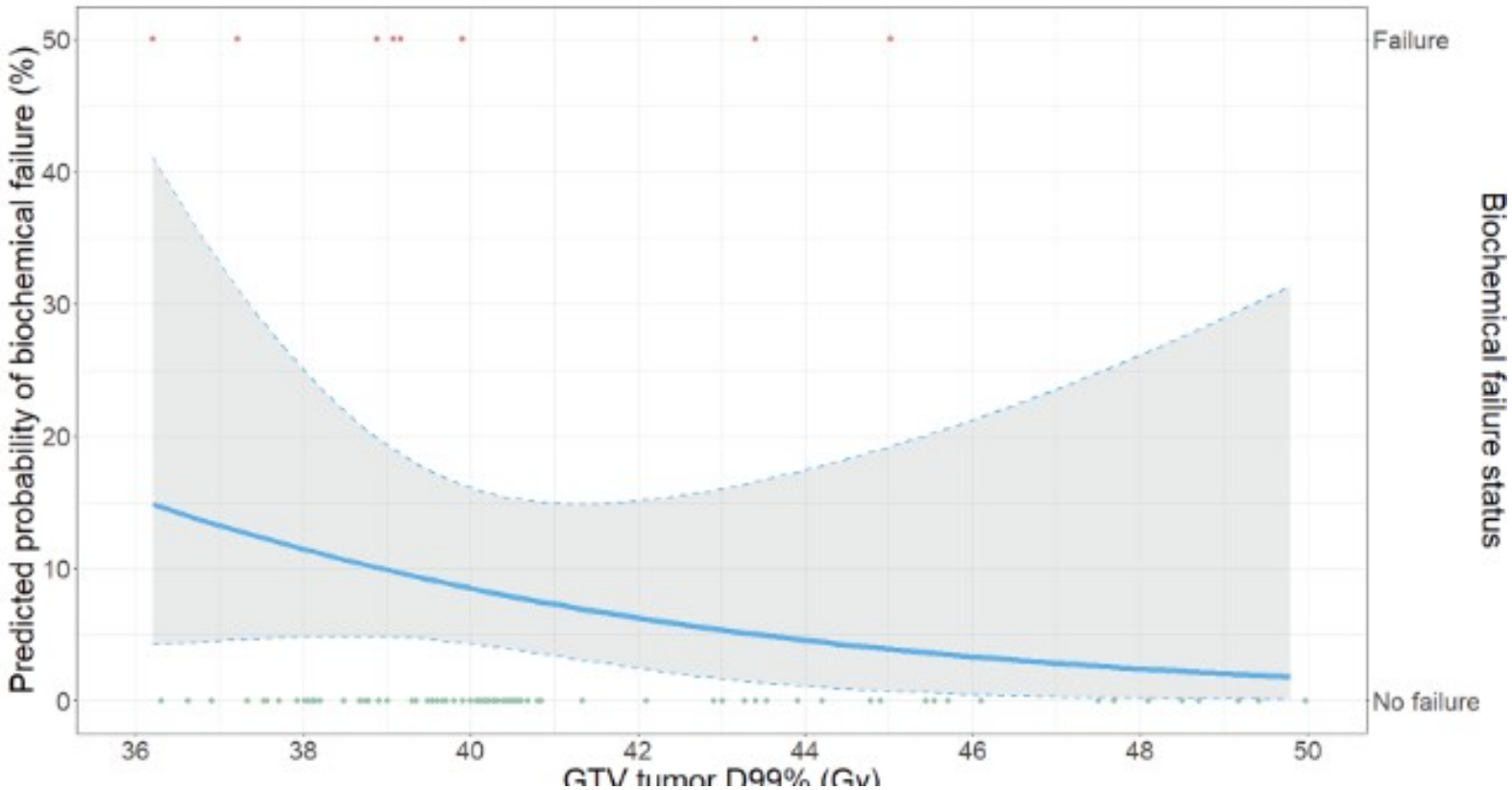


KEY RESULT - FAILURE

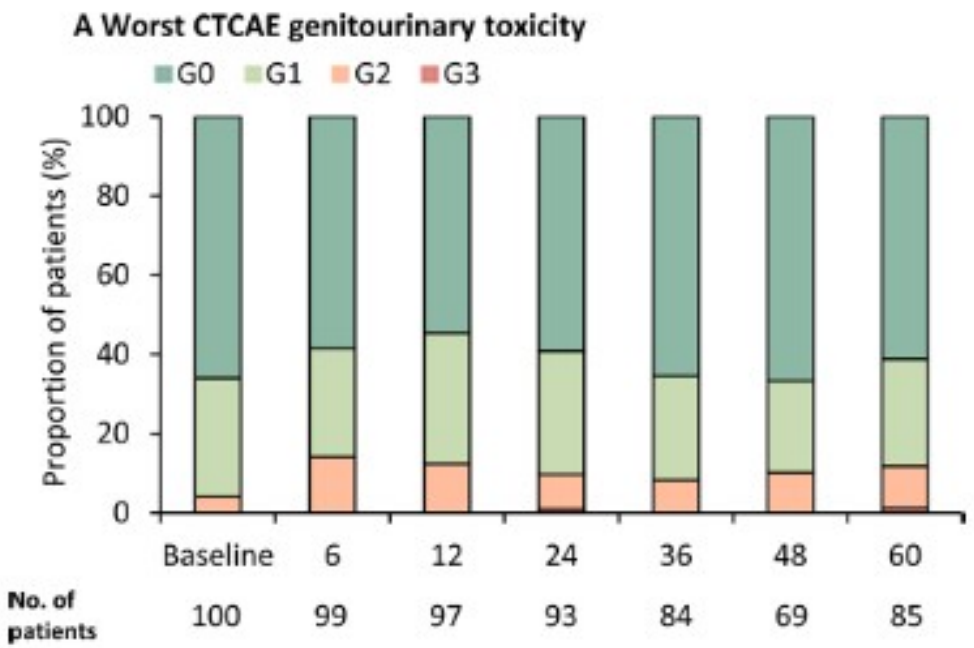
Higher GTV D99 (near-minimum dose)

correlated with

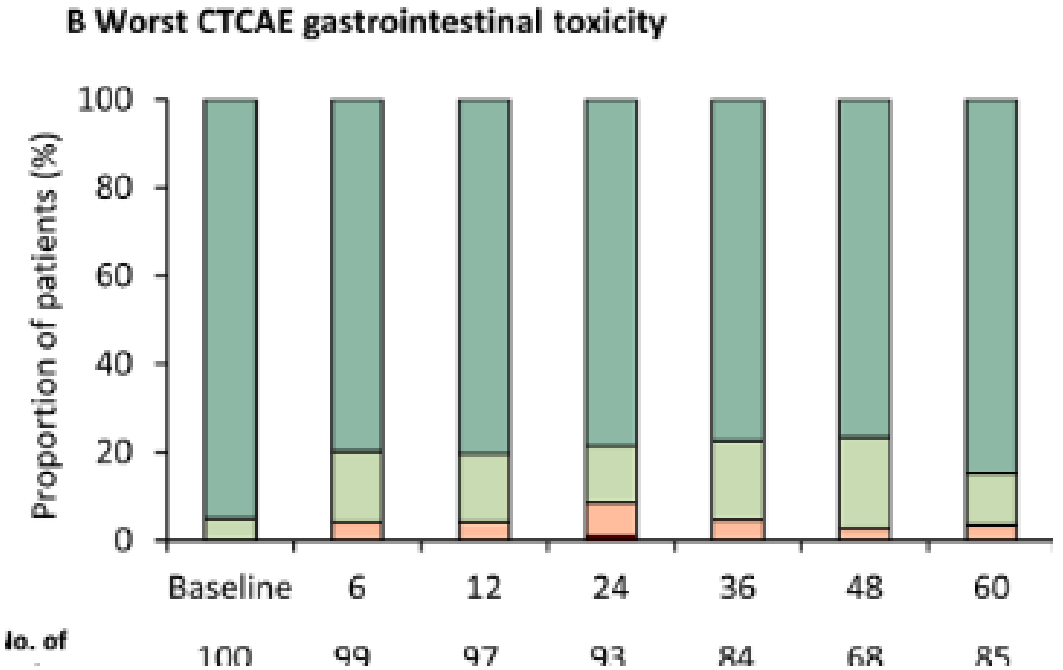
Reduced biochemical failure



KEY RESULT - TOXICITY



Gr III Toxicity (Cumulative) = 2%
Gr II Toxicity (60 months) = 12%



Gr III Toxicity (Cumulative) = 1%
Gr II Toxicity (60 months) = 4%

KEY RESULT – RETURN OF FUNCTION

BLADDER

Mean HRQoL score due to urinary bother was back to baseline after 6 months.

BOWEL

Significant difference between the bowel function HRQoL mean score at baseline compared with 5 years after treatment (p = 0.014).

SEXUAL ACTIVITY

No significant difference between the sexual activity mean score at baseline compared to the 5-year value.

STUDY - STRENGTH

1. **High-Risk Focus:** 75% high-risk cohort vs. PACE-B (intermediate-risk).
2. **Focal Boost Integration:** Achieved median GTV Dmean = 44.7 Gy without increased toxicity.
3. **Synergy with ADT:** Potential contributor to high bDFS.

Comparison to FLAME Trial:

Hypo-FLAME: 93% bDFS (5-year) vs. FLAME: 92% (conventional RT + 95 Gy boost).

STUDY - WEAKNESS

1. **Non-Randomized Design:** Selection bias possible.
2. **GTV Delineation:** Imperfections in mpMRI-based targeting.
3. **Whole-Gland Dose:** 35 Gy (lower than NCCN-recommended 36.25 Gy).

CONCLUSION

Hypo-FLAME demonstrates:

- **93% 5-year bDFS** in predominantly high-risk patients.
- **Low late toxicity** comparable to non-boosted SBRT.

Supports **focal boosting** as a strategy to enhance SBRT efficacy without compromising safety.

Final Message:
“Hypo-FLAME bridges ultra-hypofractionation and focal escalation, offering a promising paradigm for high-risk prostate cancer.”

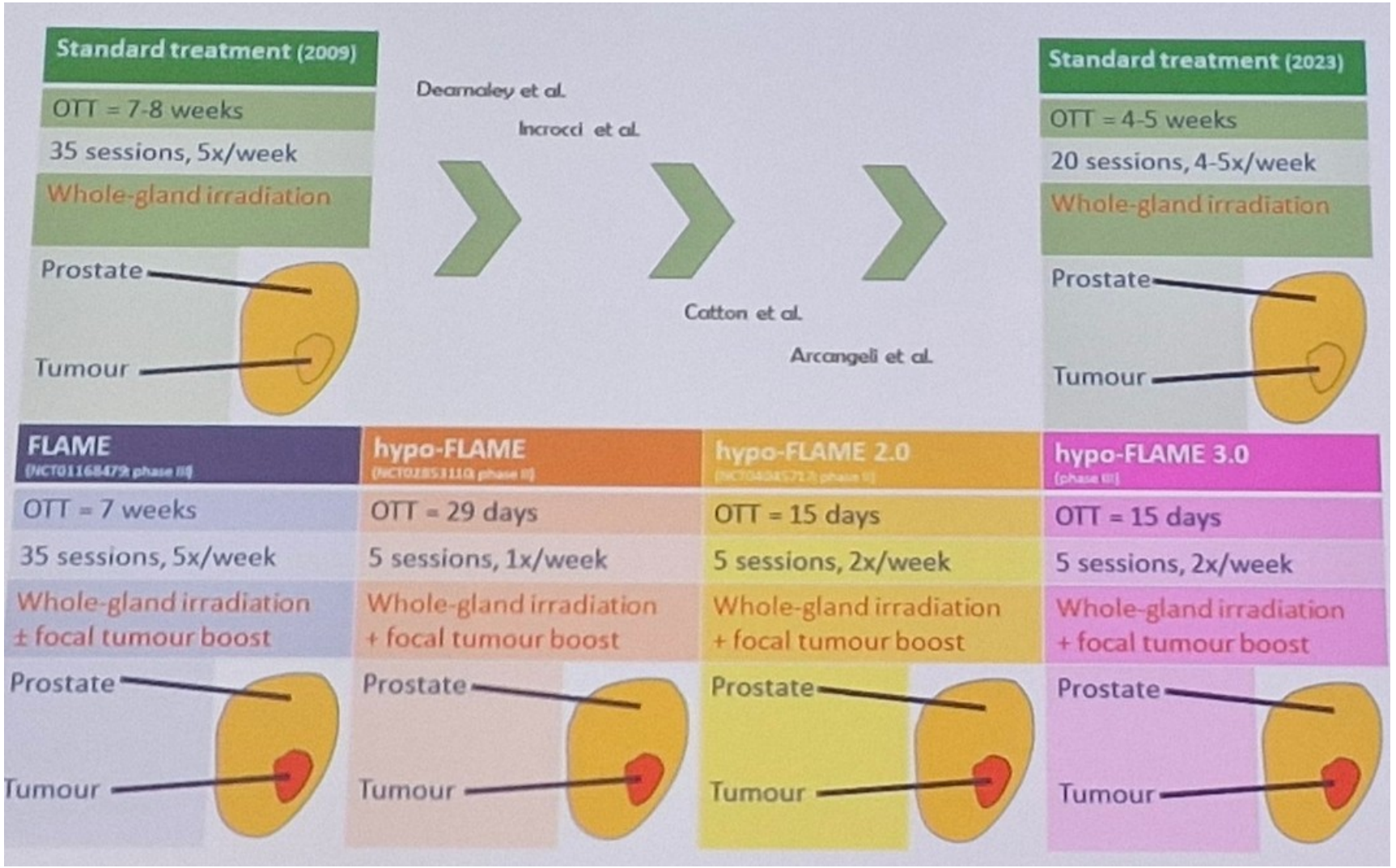
CLINICAL IMPLICATIONS

1. **For High-Risk Patients:** Ultra-hypofractionated SBRT + focal boost is feasible with excellent 5-year outcomes.

2. **Balancing Efficacy/Safety:** Iso-toxic boosting prioritizes OARs, enabling safe dose escalation.

3. **Cost/Logistics:** Reduces treatment sessions vs. conventional RT.

FUTURE DIRECTION



THANK YOU

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HYPO FLAME VS PACE B VS FLAME

Aspect	Hypo-FLAME Trial	PACE-B Trial	FLAME Trial
Design	Phase II, prospective, multicenter	Phase III, randomized, non-inferiority	Phase III, randomized
Patient Risk	75% high-risk, 25% intermediate-risk	Low- and intermediate-risk	Intermediate- and high-risk
Radiation Dose	Whole gland: 35 Gy in 5 fx Boost: Up to 50 Gy	Whole gland: 36.25 Gy in 5 fx (no boost)	Whole gland: 77 Gy in 35 fx Boost: Up to 95 Gy
Fractionation	Ultra-hypofractionated (5 fractions)	Ultra-hypofractionated (5 fractions)	Conventional (35 fractions)
5-Year bDFS	93% (95% CI: 86–97%)	95.7% (non-boosted, intermediate-risk)	92% (boosted arm)
Late Toxicity (Grade ≥2)	GU: 12% GI: 4% (CTCAE v4.0)	GU: 5–10% GI: 1–5% (RTOG grading)	GU: 23% GI: 12% (CTCAE)
ADT Use	62% received ADT	Minimal (lower-risk cohort)	Common (high-risk cohort)
Key Innovation	SBRT + iso-toxic focal boost in high-risk patients	Validated SBRT for low/intermediate risk	Conventional RT + focal boost for dose escalation
Strengths	High-risk focus; safe dose escalation	Non-inferiority of SBRT vs. conventional RT	Improved bDFS with focal boost
Limitations	Non-randomized; lower whole-gland dose (35 Gy)	Excluded high-risk patients; no boost	Higher toxicity vs. SBRT trials