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Randomized Controlled Trial of Hypofractionated vs. Normo-Fractionated Accelerated Radiation Therapy with or without Cisplatin for Locally Advanced Head and Neck Squamous Cell Carcinoma (HYPNO)

Presented by:

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Disclosure & Study Team

- Disclosure: I have no conflicts of interest to disclose.
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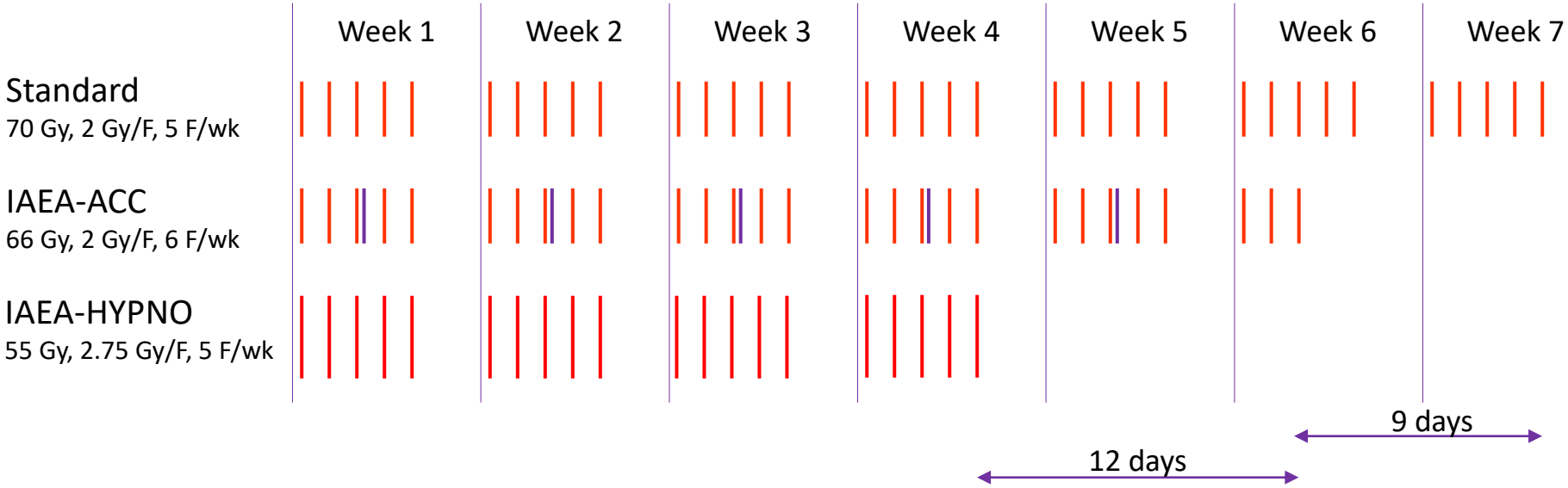
Background

- Each year 10 million deaths worldwide are attributed to cancer. 7 million of these occur in low- and middle-income countries (LMIC).
- Head and neck cancer is the sixth most common cancer worldwide (4.5% of new cases) but affects low- and middle-income countries disproportionately. In India, for example, HNSCC constitutes 30% of incident cancers.
- Patients in LMIC generally have limited access to radiation therapy (and to surgery!).
- Reducing the number of radiation dose-fractions would allow more patients to be treated.

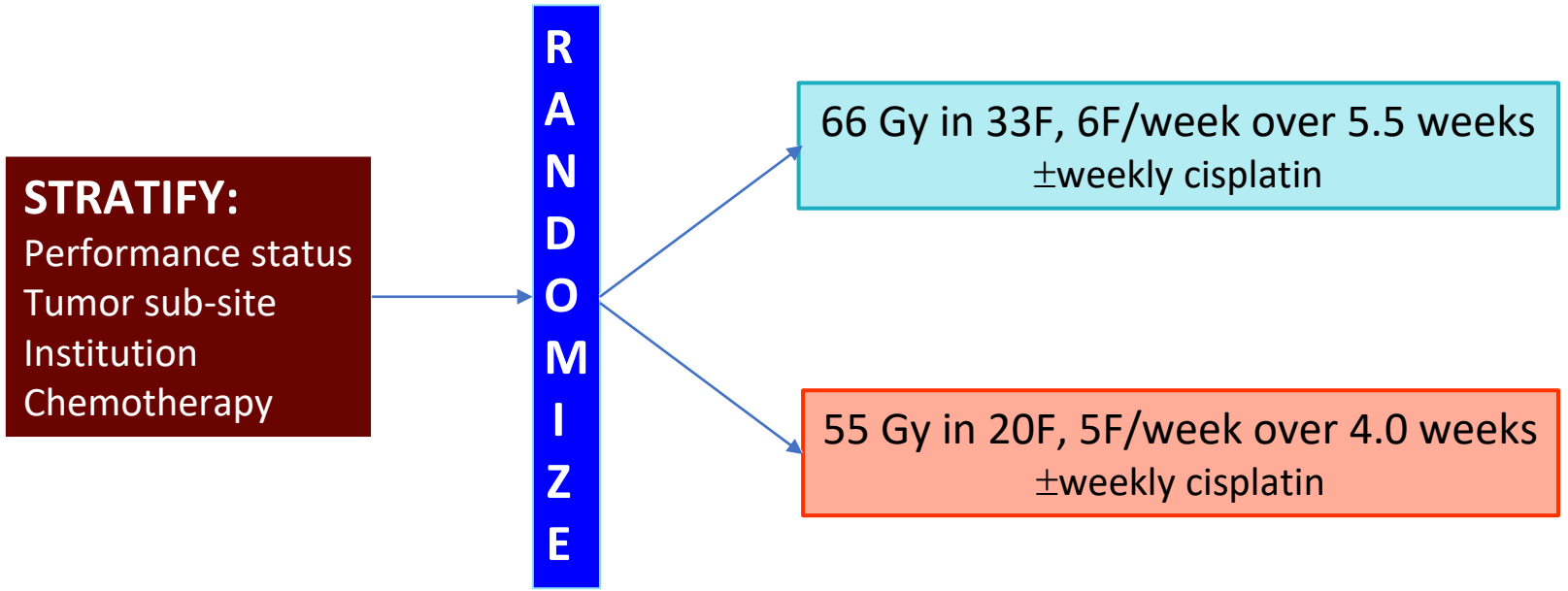
Fewer, larger fractions

We used mathematical models to analyze outcomes of published randomized controlled trials. Our modeling predicted, a 20-fraction, 4-week schedule could provide non-inferior outcomes for both tumor control and late adverse events compared with a ‘standard’ 35-fraction, 7-week schedule.



Method

Stratified, randomized controlled open-label non-inferiority phase III trial



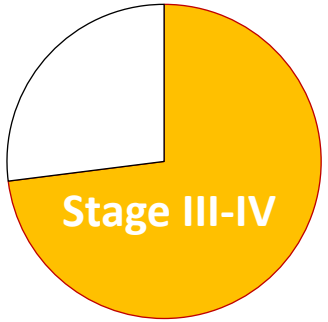
Co-primary endpoints: loco-regional tumor control
Grade 3+ late adverse events

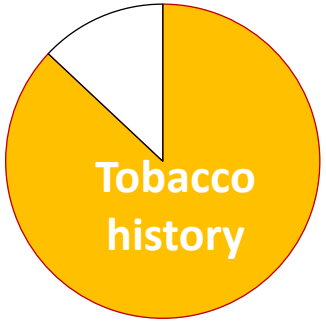
H0: Hypo-Fx non-inferior for BOTH primary endpoints, with non-inferiority margin: Δ=10%

The HYPNO trial – sponsor

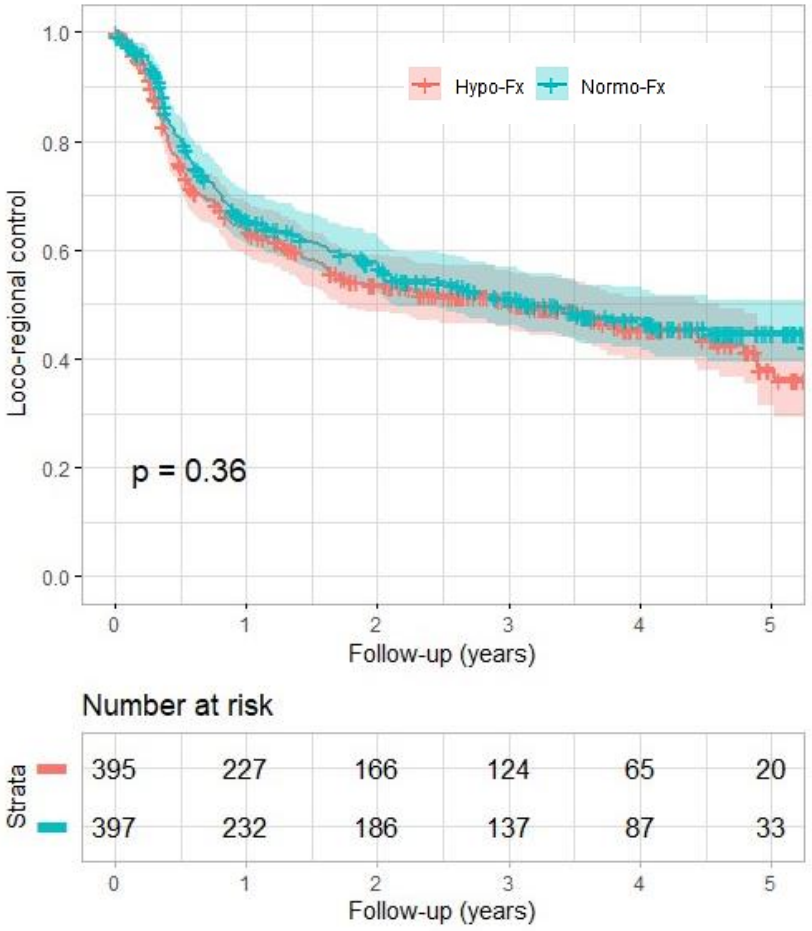
IAEA International Atomic Energy Agency

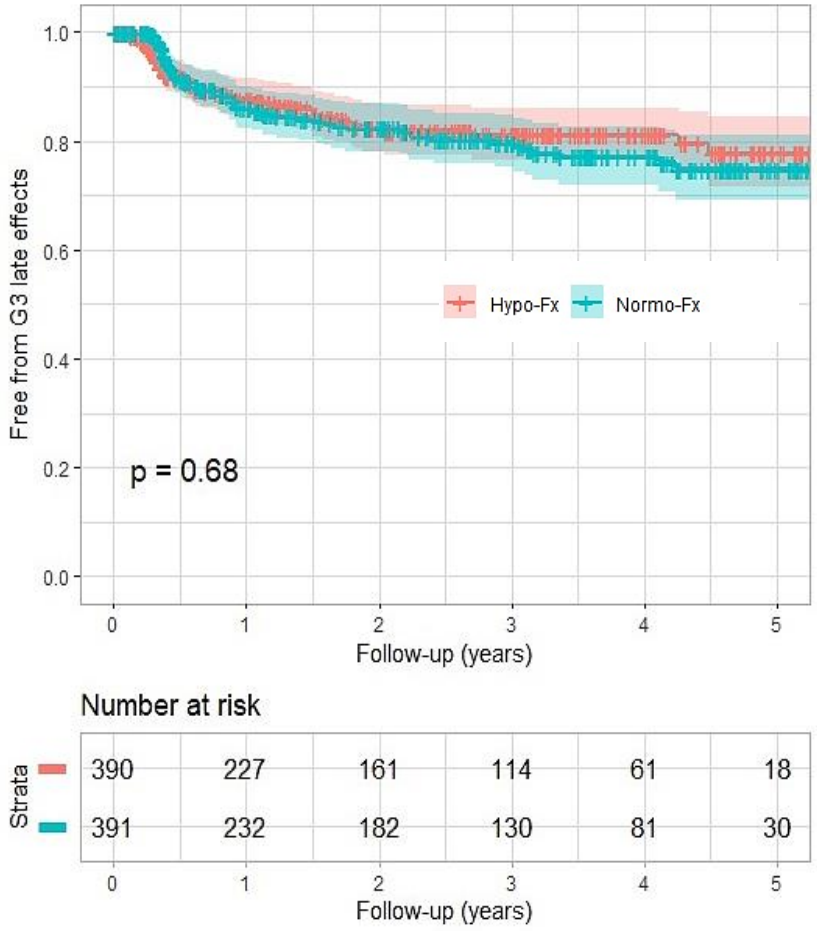
- **792 patients** with locally advanced head and neck cancer randomized
- 12 centers, 10 low- and middle-income countries, 4 continents

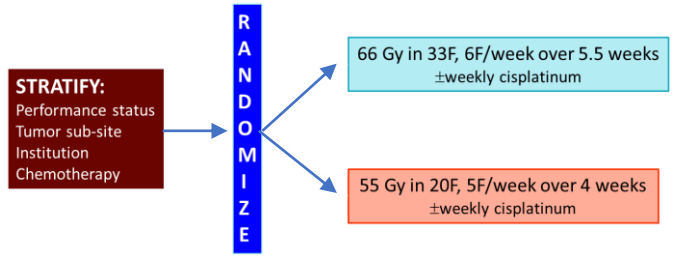




Results: tumor effect & adverse events





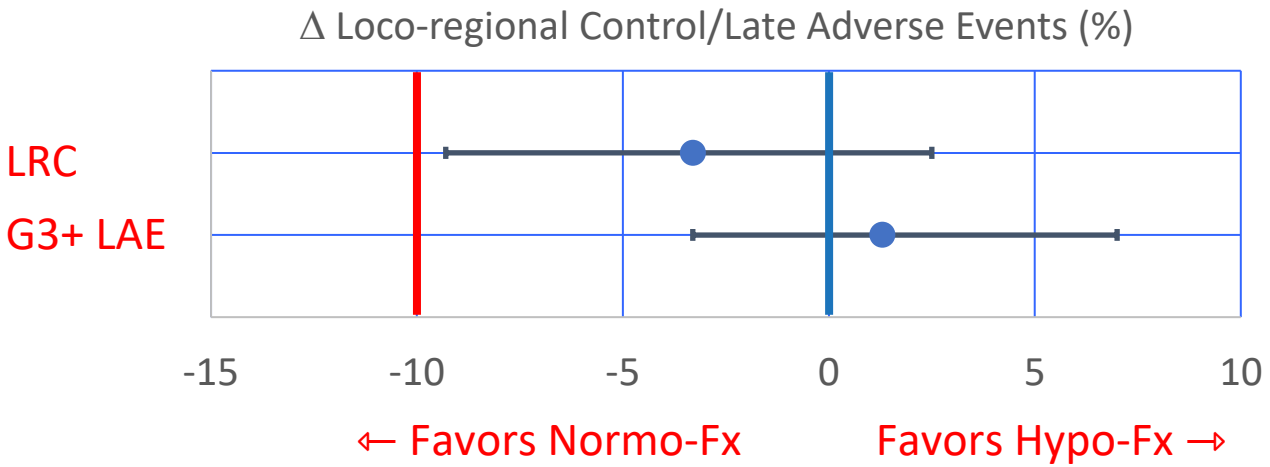


3-year outcome

	LRC
Hypo-Fx	50.7±2.7%
Normo-Fx	51.2±2.7%
P-value	0.36

	Late Grade 3+ AEs
Hypo-Fx	18.8±2.4%
Normo-Fx	20.2±2.4%
P-value	0.68

Results: Non-inferiority & Survival

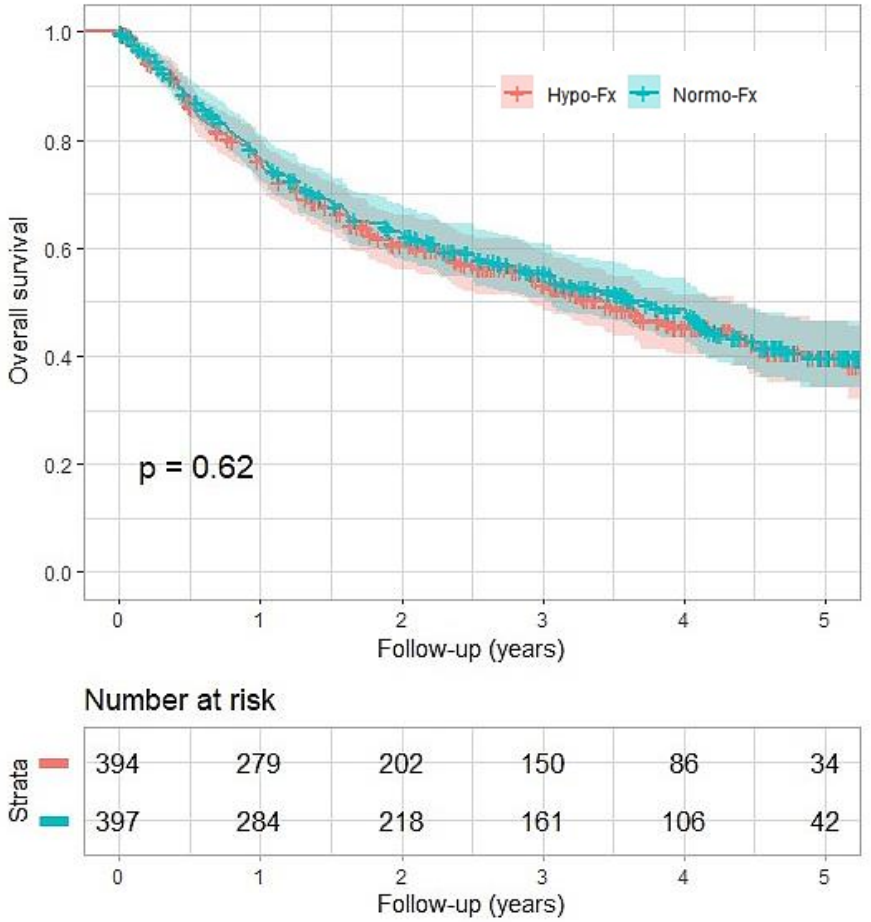


PRIMARY ANALYSIS

Non-inferiority tests:

Loco-regional control: P=0.04

Grade ≥3 late adverse events: P=0.004



Conclusions

- Large RCT (N=792) testing a hypothesis derived from mathematical modeling of clinical trial data.

- Pragmatic randomized trial conducted in low- and middle-income countries with high incidence and mortality of HNSCC with the aim of informing health care in these populations.

- Resource-sparing Hypo-Fx ± weekly cisplatin is *non-inferior* to accelerated RT with 6/F per week with respect to BOTH adverse events and tumor control.

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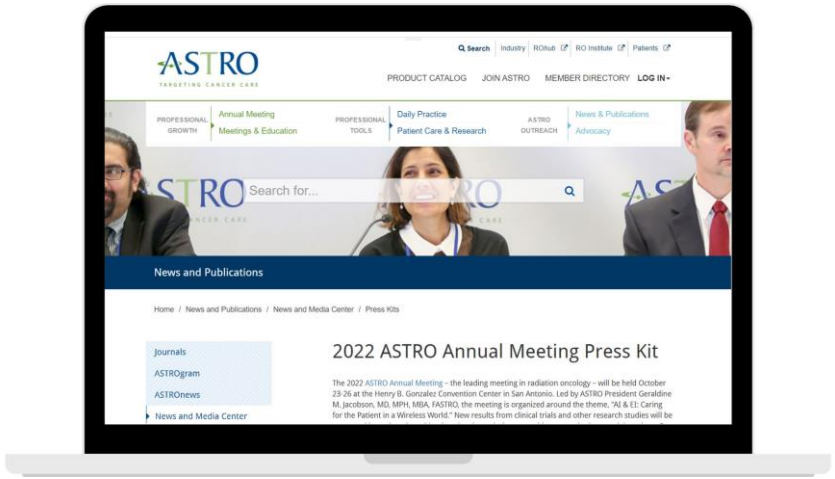

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