

Salvage surgery and Intraoperative electron beam radiotherapy for locoregionally persistent or recurrent head and neck cancer: single institution study

Dukagjin M. Blakaj, MD PhD

Professor

Vice Chair of Clinical Operations

Director of H&N/Skull Base Division

Director of CNS/Peds & H&N IORT Fellowships

Department of Radiation Oncology

Background

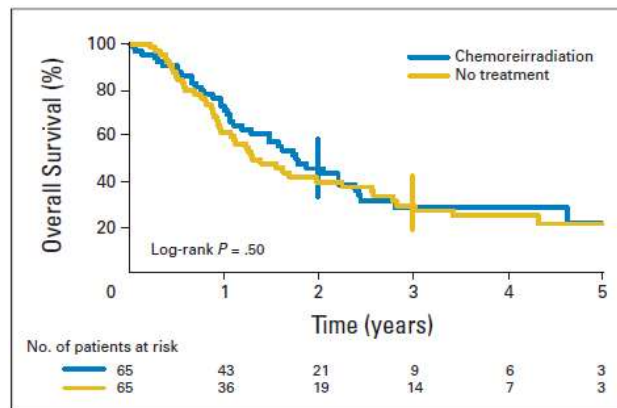
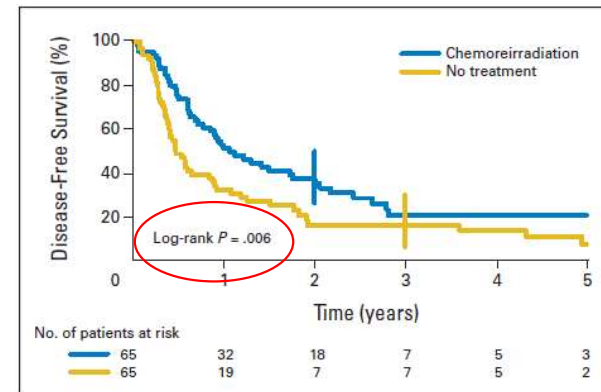
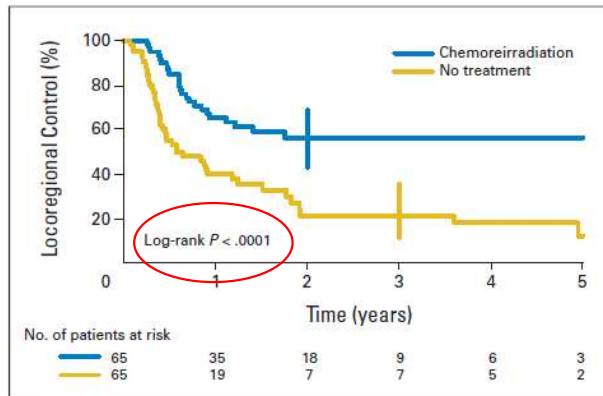
- Standard of care for locoregionally recurrent head/neck cancer is surgical resection with adjuvant therapy.
- Local control after surgery alone is unacceptably low. Post-op chemoradiation has been shown to improve LC and PFS.
- Local failure remains the primary site of recurrence and overall prognosis is very poor.
- IORT may play a role in improving local control and decreasing toxicity for these patients.

Randomized Trial of Postoperative Reirradiation Combined With Chemotherapy After Salvage Surgery Compared With Salvage Surgery Alone in Head and Neck Carcinoma

François Janot, Dominique de Raucourt, Ellen Benhamou, Christophe Ferron, Gilles Dolivet, René-Jean Bensadoun, Marc Hamoir, Bernard G ry, Morbize Julieron, Marine Castaing, Etienne Bardet, Vincent Gr goire, and Jean Bourhis

- 130 previously radiated patients with recurrent head/neck cancer
- Randomized to surgery followed by:
 - Observation
 - Chemoradiation
 - 60 Gy with concurrent 5-FU and Hydroxyurea

Results



Toxicity

| Table 3. Late Toxicity at 1 and 2 Years After Random Assignment | | | | |
|-----------------------------------------------------------------------------|----------------------------------|-----|----------------------------------|----|
| Toxicity | RT Arm (n = 42; 1 missing) | | WS Arm (n = 33; 3 missing) | |
| | No. | % | No. | % |
| Toxicity at 12 and 12.5 months after random assignment, RTOG grade ≥ 3 | | | | |
| Mucositis | 4 | 10 | 1 | 3 |
| Skin | 0 | 0 | 0 | 0 |
| Subcutaneous tissues | 6 | 14 | 3 | 9 |
| Larynx | 0 | 0 | 0 | 0 |
| Osteoradionecrosis | 1 | 2 | | |
| Trismus | 3 | 7 | 2 | 6 |
| Pharyngeal stenosis | 1 | 2 | 0 | 0 |
| No. of patients | 11 | 26 | 3 | 9 |
| Toxicity at 24 months after random assignment, RTOG grade $\geq 3^*$ | | | | |
| Mucositis | 1 | 6 | 0 | 0 |
| Skin | 1 | 6 | 0 | 0 |
| Subcutaneous tissues | 4 | 22 | 1 | 5 |
| Larynx | 1 | 6 | 0 | 0 |
| Trismus | 5 | 28 | 2 | 10 |
| Osteoradionecrosis | 3 | 17 | 0 | 0 |
| Pharyngeal stenosis | 1 | 5.5 | 0 | 0 |
| No. of patients | 7 | 39 | 2 | 11 |

Purposes of study

1. Update our clinical outcomes using IORT for recurrent head/neck cancer.
2. Determine if surgical margin status, ENE, and other variables have a significant impact on LRC, PFS, and OS.

Patients' characteristics 2000- 2015 vs 2000-2023

Initial 61 Patients

- Median age 58.
- SCC. 74%
- +ve margin 46%

Updated 130 Patients

- Median age 62.
- SCC. 86%
- +ve margin 47%
- +ve ENE 23%

Patient and tumor characteristics (a median follow-up of 10.5 months)

| | | | |
|---------------------|-------------|-------------------|-----------|
| Age | 62 (54, 72) | Pathology | |
| Sex | | SCC | 112 (86%) |
| Female | 39 (30%) | Adenoid Cystic | 5 (3.8%) |
| Male | 91 (70%) | Mucoepidermoid | 2 (1.5%) |
| Primary Site | | EPA | 1 (0.8%) |
| Oral cav. | 35 (27%) | Sarcoma | 4 (3.1%) |
| OPC | 31 (24%) | Other | 6 (4.6%) |
| Larynx/HPC | 26 (20%) | p16 Status | |
| Salivary | 12 (9.2%) | Negative | 46 (73%) |
| Sinonasal | 14 (11%) | Positive | 17 (27%) |
| Other | 12 (9.2%) | Unknown | 67 |

Radiation details

- All 130 patients received EBRT for adjuvant or definitive aim for the primary disease (initial 1st radiation treatment).
- Median initial EBRT dose was 6600cGy.
- **IORT: for recurrent HN cancer**
- Median IORT dose was 12.5 Gy.
- Median energy used was 6MeV
- Median IDL prescription was 90% (87-100)
- Median Cone size was 6 cm (3-10) (indicator of the tumor size)

Acute toxicity (<90 days)

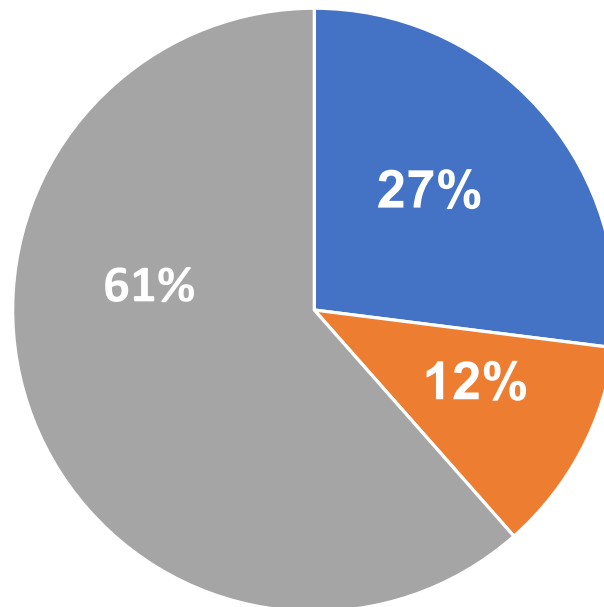
- Total patients with Acute Toxicity 26 (33%)
- Total 11 (8.5%) had \geq G3 toxicity:
 - 5 patients had wound complications, including open wound and wound dehiscence.
 - 3 patients had trachea-esophageal fistula.
 - 2 patients had moderate to severe dysphagia.
 - 1 patient had carotid blow out.

Surgical pathology details

Post IORT Margins

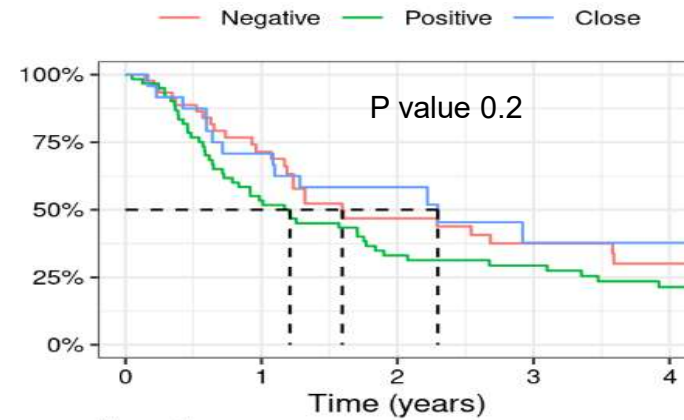
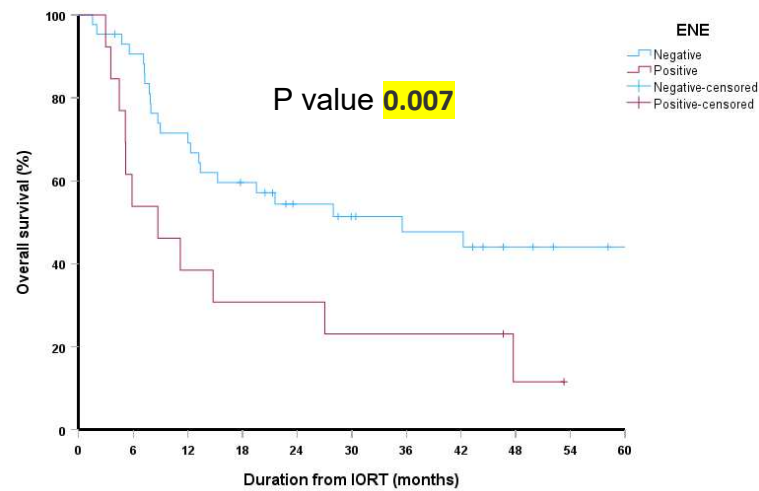
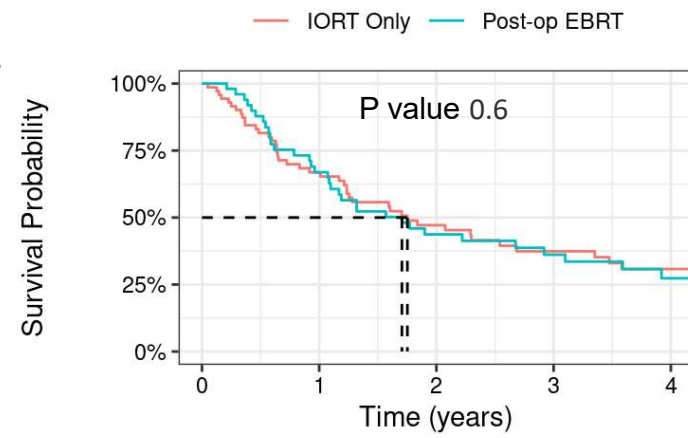
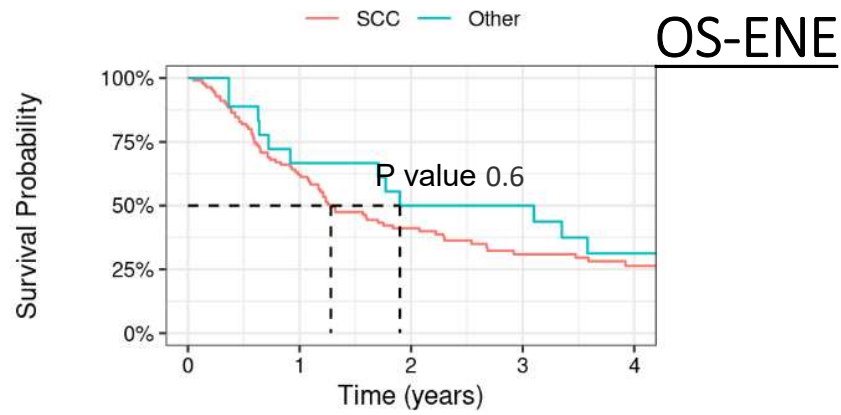
| | |
|----------------------------------|----------|
| Negative | 45 (35%) |
| Positive | 61 (47%) |
| Close | 24 (18%) |
| PNI | 67 (68%) |
| Unknown | 32 |
| LVI | 28 (36%) |
| Unknown | 52 |
| ENE (recurrence is Nodal) | 14 (23%) |

| | |
|-----------------|----------|
| IORT | 61% (80) |
| IORT+EBRT | 27% (35) |
| IORT+EBRT+Chemo | 12% (15) |

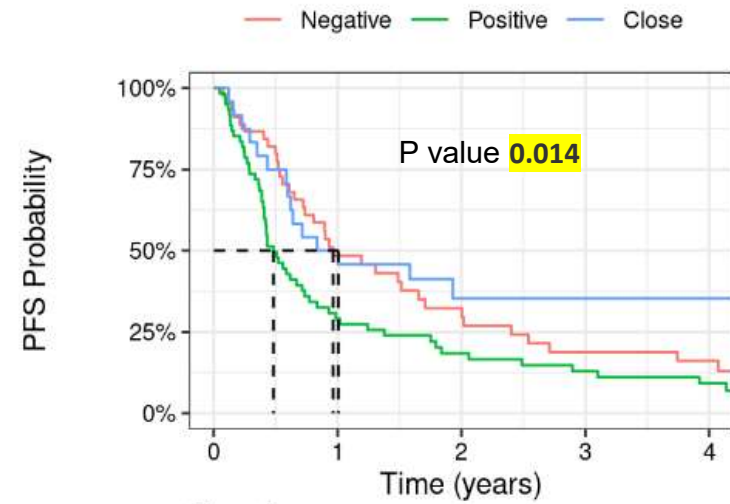
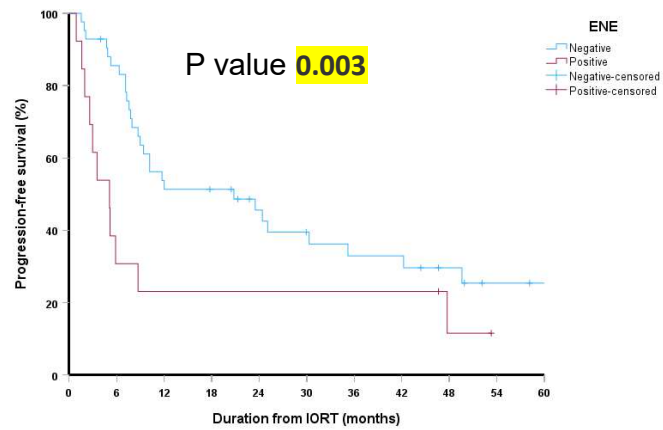
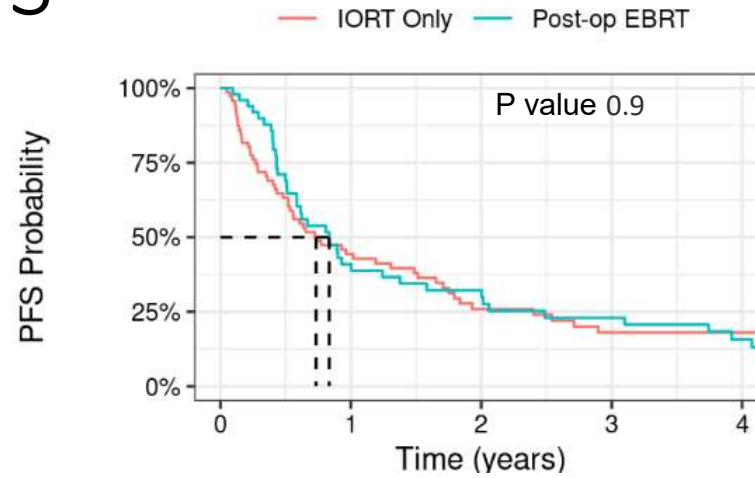
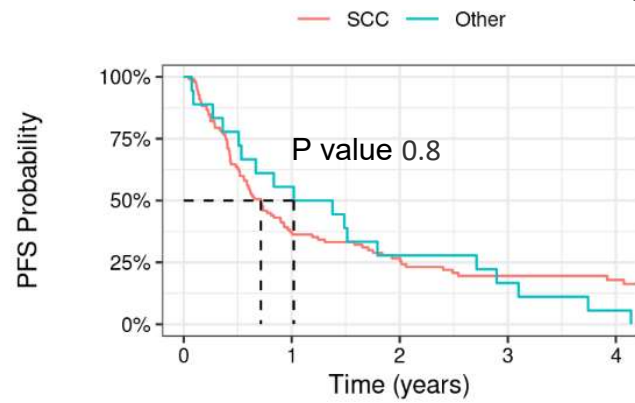


| Strata | N | Median LRC (months) | 1 Year LRC | Median PFS (months) | 1 Year PFS | Median OS (months) | 1 Year OS | 2 Year OS |
|---------------------|-----|---------------------|---------------------|---------------------|----------------------|--------------------|----------------------|-----------|
| All Patients | 130 | 18.2 | 59% | 8.7 | 40% | 18.8 | 63% | 42% |
| Pathology | | | | | | | | |
| SCC | 112 | 19.8 | 60% | 8.6 | 37% | 15.4 | 62% | 41% |
| Other | 18 | 14.4 | 56% | 14.4 | 56% | 30 | 67% | 50% |
| Margins | | | | | | | | |
| Negative | 45 | 19.8 | 68% | 11.6 | 48% | 19.1 | 71% | 47% |
| Positive | 61 | 10 | 49% | 5.8 | 29% | 14.5 | 53% | 33% |
| Close | 24 | 23.2 | 64% | 11 | 50% | 27.6 | 71% | 58% |
| ENE +ve | 15 | 9 36 | 45% vs 70%, p.33 | 6 18 | 22% vs 55%, p .02 | 12 24 | 38% vs 67%, p .01 | |
| Post-op EBRT | 50 | 19 | 62% | 10 | 41% | 20.5 | 67% | 44% |
| IORT Only | 71 | 14.3 | 54% | 8.8 | 44% | 21 | 67% | 47% |

Equivalent OS and PFS

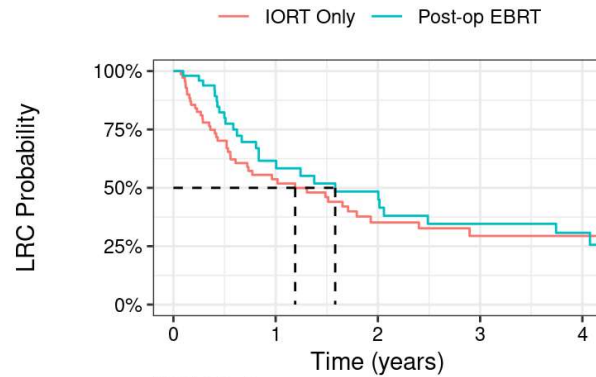


PFS



IORT only vs IORT+ EBRT

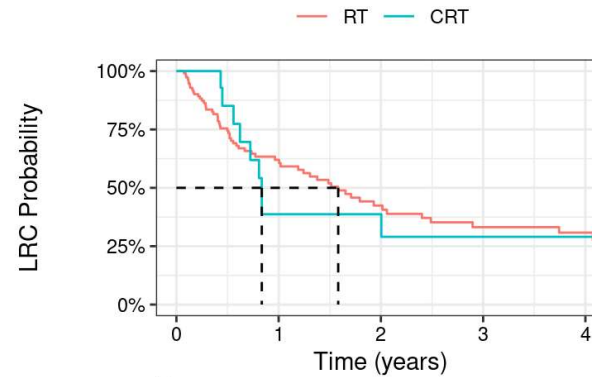
p NS



| | | | | | |
|--------------|----|----|----|----|----|
| IORT Only | | | | | |
| At Risk | 71 | 29 | 14 | 9 | 6 |
| Censored | 0 | 12 | 18 | 21 | 24 |
| Events | 0 | 30 | 39 | 41 | 41 |
| Post-op EBRT | | | | | |
| At Risk | 50 | 19 | 14 | 10 | 6 |
| Censored | 0 | 15 | 16 | 16 | 19 |
| Events | 0 | 16 | 20 | 24 | 25 |

IORT only vs. IORT +CRT

p NS



| | | | | | |
|----------|-----|----|----|----|----|
| RT | | | | | |
| At Risk | 113 | 44 | 24 | 16 | 10 |
| Censored | 0 | 31 | 38 | 41 | 46 |
| Events | 0 | 38 | 51 | 56 | 57 |
| CRT | | | | | |
| At Risk | 15 | 4 | 4 | 3 | 2 |
| Censored | 0 | 3 | 3 | 3 | 4 |
| Events | 0 | 8 | 8 | 9 | 9 |

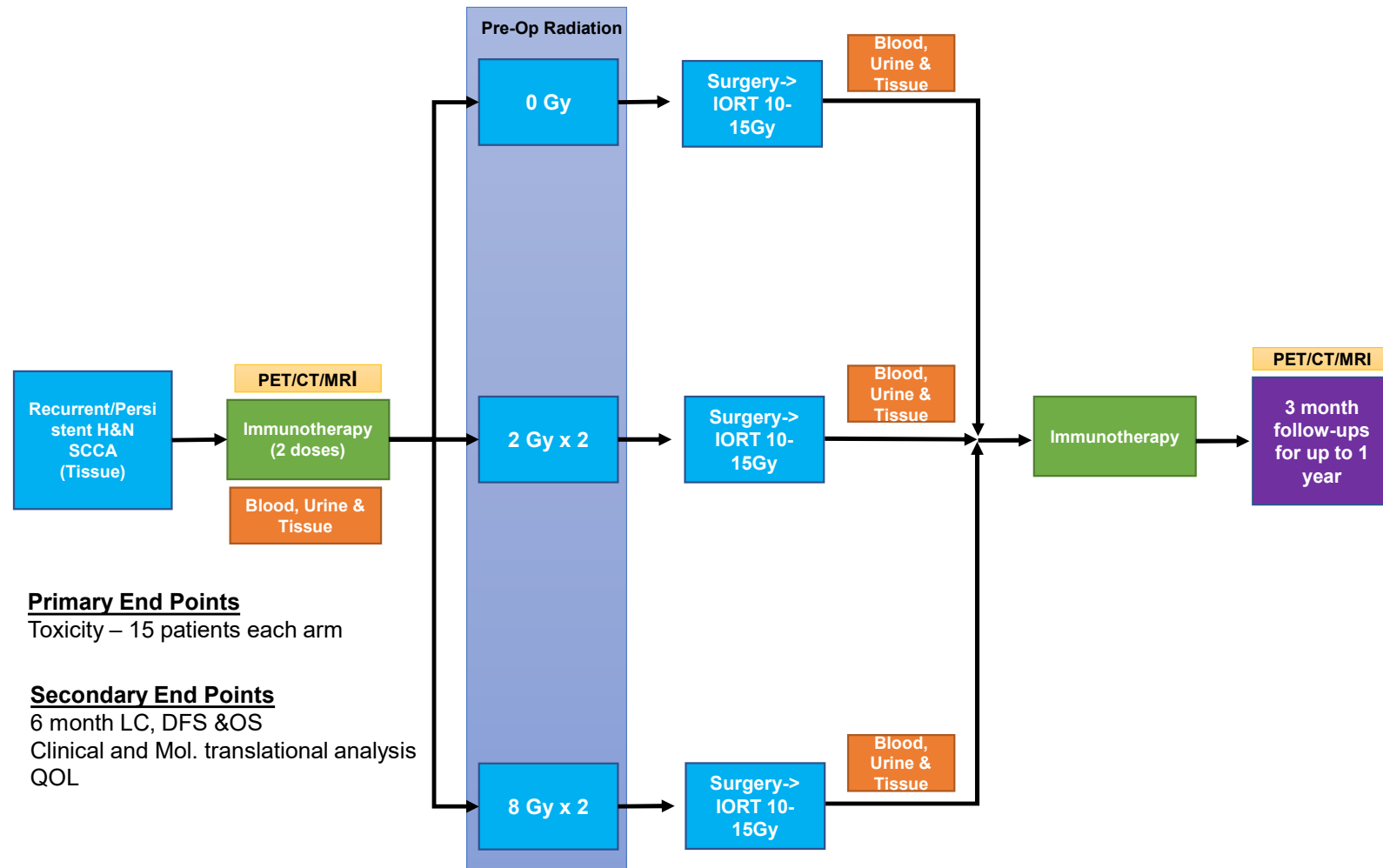
Conclusions

- In a population of previously radiated recurrent H&N cancer patients, IORT achieved 1 and 2-year OS rates comparable to the French trial, despite only ~40% receiving post-operative RT and ~11.5% receiving post-op chemoRT.
- Advantages of IORT decreased toxicity, decrease duration of post-op treatment.
- Manuscript is in preparation

Future Directions

- Pool H&N salvage IORT data with other institutions to increase our numbers
- Prospective protocol looking at the safety and efficacy of salvage surgery/IORT with and followed by immune therapy.
 - Hypothesis: Adding IO and pre op RT to IORT will improve upon our LC and PFS outcomes

HNSALV Trial



Acknowledgments

- Arnab Chakravarti MD
 - John Grecula MD
- Ahmed Elguindy MD, PhD (soon)
 - Mauricio Gamez MD
 - Patrick Wald MD
- Nikol Mladkova MD PhD
 - Marcelo Bonomi MD
- James Rocco MD PhD
 - Matt Old MD
 - Enver Ozer MD
- Amit Agrawal MD
- Steven Kang MD
- Ricardo Carrau MD
 - Nolan Seim MD
- Kyle VanKoeveering MD



THANK YOU!

