867P: A phase I trial of *nab*-paclitaxel based induction followed by *nab*-paclitaxel based concurrent chemotherapy and re-irradiation in previously treated head and neck squamous cell carcinoma

Ari J. Rosenberg[1,2], Nishant Agrawal[1,3], Zhen Gooi[1,3], Elizabeth Blair[1,3], Louis Portugal[1,3], David Chan1,3, Alexander Pearson[1,2], Aditya Juloori[1,4], Jeffrey Chin[1,2], John Cursio[1,5], Mark Lingen[1,6], Daniel Haraf[1,4], Everett E. Vokes[1,2]

[1]University of Chicago, Chicago, IL, USA; [2]Section of Hematology/Oncology; [3]Otolaryngology-Head and Neck Surgery; [4]Radiation and Cellular Oncology; [5]Public Health Sciences, [6]Pathology

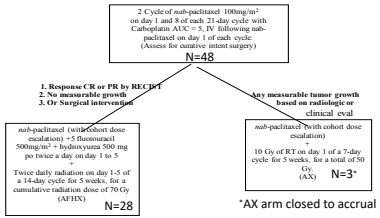
arirosenberg@medicine.bsd.uchicago.edu

Introduction

- Recurrent head and neck squamous cell carcinoma (HNSCC) is generally treated palliatively with immunotherapy-based treatment, yet survival remains poor.
- Re-irradiation is an aggressive but potentially curative salvage approach in this setting.
- This study evaluated nab-paclitaxel based re-induction and re-irradiation with concurrent nab-paclitaxel-based chemotherapy in recurrent HNSCC.
- We report the primary analysis and outcomes.

Methods

- Eligible patients had recurrent or second primary HNSCC requiring locoregional therapy not amenable to surgical salvage in patients with previously irradiated HNSCC.
- *Nab*-paclitaxel and carboplatin re-induction were administered for 2 cycles.
- Complete response (CR), partial response (PR), or stable disease (SD) received *nab*-paclitaxel on day 1 with cohort dose escalation in combination with 5-fluorouracil, and hydroxyurea with twice daily radiation on days 1-5 of a 14-day cycle for 5 cycles for a cumulative radiation dose of 75 Gy (AFHX). Progressive disease (PD) received palliative radiation.
- The primary endpoint was maximally tolerated dose and dose limiting toxicity of nab-paclitaxel when given with AFHX. Secondary endpoints included progression free survival (PFS) and overall survival (OS).



*AX arm closed to accrual

Figure 1. Trial Schema. *CR: Complete Response; PR: Partial Response; AFHX: nab-paclitaxel, 5-fluorouracil, and hydroxyurea, with twice daily radiation in week-on week-off CRT platform; AX: nab-paclitaxel with 10Gy of RT on day 1 of a 7 day cycle for 5 weeks*

Dose Cohort	Nab-Paclitaxel (mg/m^2)	5-FU (mg/m^2)	Hydroxyurea (mg)
-1	10	600	500 bid
1	20	600	500 bid
2	30	600	500 bid
3	55	500	500 bid
4	70	500	500bid
5	85	500	500bid
6	100	500	500bid

Table 1. Dose Escalation. *Cohorts of 3 to 6 patients treated in a standard 3 + 3 phase I study dose escalation schema.*

Conclusions

- Chemo-reirradiation is a curative salvage treatment for a subset of recurrent HNSCC.
- Response to re-induction enriches for favorable outcome.
- The role of chemo-reirradiation in the era of immunotherapy warrants investigation.

Supported by Celgene.

Results

Nab-Paclitaxel-Based Re-Induction Therapy

Characteristic	N=48
Age median, (range)	60 (27,74)
Gender	
Male	34 (70.8%)
Female	14 (29.2%)
Race	
African-American	5 (10.4%)
Caucasian	41 (85.4%)
Other	2 (4.2%)
BMI median, [IQR]	25.4,(21.3,28.2)
Characteristic	N=48
Smoking History, Pack Years	
Never Smoker	23 (47.9%)
<=10 PY	7 (14.6%)
>10 PY	17 (35.4%)
Unknown	1 (2.1%)
Disease State	
Recurrent	40 (80.3%)
Primary	7 (14.6%)
Metastatic	1 (2.1%)
p16+	14 (29.2%)
ECOG PS	
1	26 (54.2%)
0	20 (40.7%)
Unknown	2 (4.2%)

Table 1. Patient Characteristics.

- Seventeen patients discontinued prior to re-irradiation (n=17)
  - Progressive disease (n=7)
  - Death due to infection (n=3)
  - Continued off-protocol (n=2)
  - Transitioned to hospice (n=3)
  - Withdrew consent (n=2)

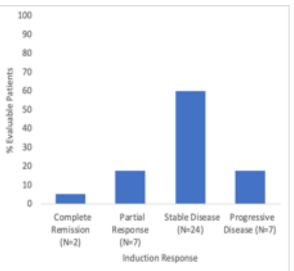


Figure 2. Response to re-induction.

AFHX Re-irradiation Therapy

- From March 2013 until January 2020, 48 patients (pts) were eligible and started re-induction, and 28 pts started AFHX.
- Median follow-up 5.6 years.
- The maximally tolerated dose (MTD) and recommended phase II dose (RP2D) for *nab*-paclitaxel with AFHX re-irradiation therapy was determined to be 100 mg/m2.
- Overall, estimated four-year progression free survival (PFS) and overall survival (OS) is 22.5% and 25.7%, respectively.
- Among patients who started AFHX re-irradiation, four-year PFS and OS is 37.7% and 44.0%, respectively.

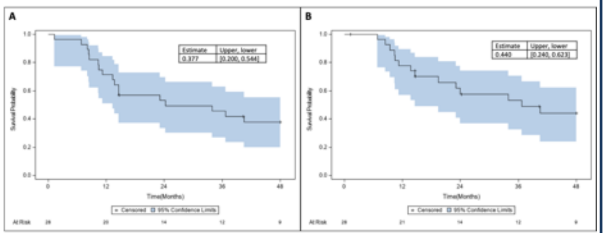


Figure 4. PFS (A) and OS (B) for patients who started AFHX re-irradiation.

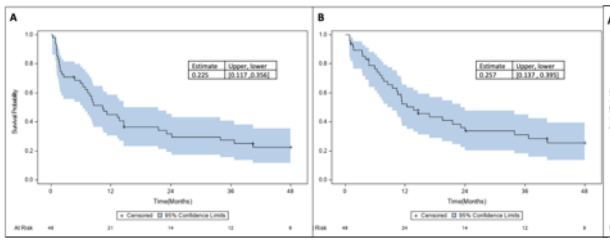


Figure 3. Progression free survival (PFS) and overall survival (OS) for the total cohort.

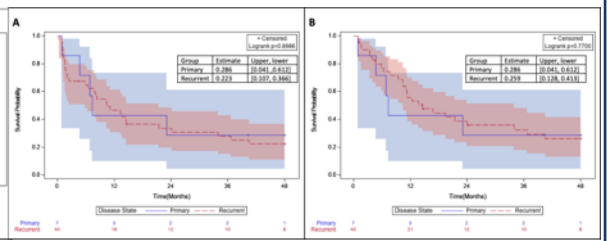


Figure 5. PFS (A) and OS (B) by disease setting. *Second primary (blue); recurrent disease (red)*