Universitätsmedizin Essen

# 618P: OPTIM - A randomized phase II study on the OPTimization of IMmunotherapy in squamous carcinoma of the head and neck - AIO-KHT-0117

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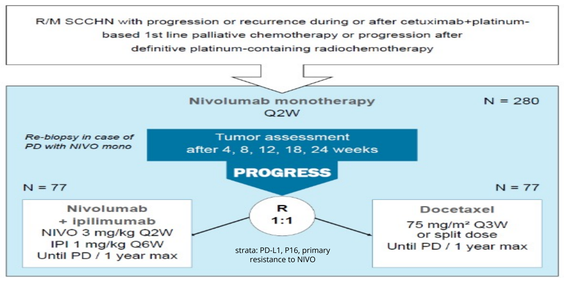
## Background

While check point inhibitors (CPI) that target PD-1 are a standard of care in recurrent or metastatic SCCHN (R/M-SCCHN), the role of CPI targeting anti-CTLA-4 remains uncertain. We evaluated whether staggered escalated immunotherapy targeting PD-1 and CTLA-4 is superior to docetaxel (DOCE) in nivolumab-refractory patients (pts).

## Methods




trial identifier: NCT03620123

Support was received from BMS for drug and funding (CA209-998)

### Trial design and population

This open-label randomized phase II trial compared efficacy and safety of nivolumab + ipilimumab (NIVO-IPI) to docetaxel (DOCE) in pts with RM-SCCHN or carcinomas of the nasal sinus. Adult pts with measurable disease and progression after platin and NIVO therapy were 1:1 randomized to:

- NIVO 3mg/kg Q2W + IPI 1mg/kg Q6W i.v. or
- DOCE 75 mg/m2 Q3W i.v.

### Analyses

Primary endpoint was objective response rate (ORR) according to RECIST 1.1. Sample size was N=154 randomized pts. (1-sided $\alpha$= 0.05, P80%).
FPI was JUL 2018. Early termination occurred in FEB 2020 due to change of treatment landscape. Descriptive analyses and KM-plots were applied and included progression-free survival (PFS), overall survival (OS) and safety (adverse events (AE) according to CTCAE V4.03).

## Results

The majority of 31 randomized pts. had tobacco exposure (80.6%), P16-negative OPC (25.8%) and TPS positive disease (51.6%)

- Extents of exposure for NIVO, IPI and DOCE were:
  - Median cycles: 3.5, 1.5 and 5.
  - Planned doses: 95.6%, 94.0% and 95.1%
- ORR was 0% vs. 17.6% for IPI + NIVO vs. DOCE
- PFS favored DOCE (1.97 mo. (95%CI,1.25-2.36) vs. 3.66 mo. (95%CI, 1.25-2.3); P=.036)
- $PFS_{6mo.}$ was 7.1% vs. 25.0% for NIVO-IPI vs. DOCE
- OS showed a trend favoring DOCE (3.97mo. (95%CI, 1.64-18.6) vs. 11.9 mo. (95%CI, 1.84-21.0); P=.356)
- $OS_{12mo.}$ was 28.6% vs. 44.6% for NIVO-IPI vs. DOCE
- TRAE favored NIVO-IPI (38.5% (16.6-64.5) vs. 68.8% (17.8-60.9))
- Discontinuation due to AE occurred in 7.7% and 18.8% for NIVO-IPI vs. DOCE, respectively
- Treatment–related SAE favored NIVO-IPI (7.7% (diarrhea)) vs. DOCE (25.0% (asthenia, colitis, pneumonia, sepsis, syncope))

## Conclusion

- OPTIM is the first randomized trial to assess NIVO-IPI as 3rd line treatment (after NIVO- and platinum-failure) in pts. with RM-SCCHN
- Major limitations were the small number of randomized pts and the predominance of adverse factors (tobacco exposure, P16-negative OPC and early failure after radiochemotherapy)
- No new safety signal was reported for NIVO-IPI and the safety profile was consistent with previous reports
- The addition of IPI to NIVO did not salvage NIVO-refractory RM-SCCHN pts
- Efficacy parameter favored DOCE and underscored the relevance of chemotherapy as 3rd line treatment in RM-SCCHN pts

**Table 1: Patients demographics**

| | Nivolumab + Ipilimumab (n=14) | Docetaxel (n=17) | Total (N=31) |
|---|---|---|---|
| **age** | | | |
| **median (range), years** | 63.5 (51-84) | 64.0 (39-81) | 64.0 (39-84) |
| **male, % (n)** | 64.3 (9) | 76.5 (13) | 71.0 (22) |
| **Caucasian, % (n)** | 100.0 (14) | 100.0 (14) | 100.0 (14) |
| **Tobacco-use** | | | |
| **current or former, % (n)** | 78.6 (11) | 82.4 (14) | 80.6 (25) |
| **never, % (n)** | 21.4 (3) | 11.8 (2) | 16.1 (5) |
| **unknown, % (n)** | 0 (0) | 5.9 (1) | 3.2 (1) |
| **median pack years (IQR)** | 25.0 (3.0-40.0) | 35.0 (7.0-50.0) | 30.0 (4.0-50.0) |
| **ECOG performance status** | | | |
| **0, % (n)** | 28.6 (4) | 17.6 (3) | 22.6 (7) |
| **1, % (n)** | 71.4 (10) | 82.4 (14) | 77.4 (24) |
| **site of primary tumor** | | | |
| **Oropharynx (OPC), % (n)** | 35.7 (5) | 41.2 (7) | 38.7 (12) |
| **oral cavity, % (n)** | 42.9 (6) | 5.9 (1) | 22.6 (7) |
| **hypopharynx, % (n)** | 14.3 (2) | 23.5 (4) | 19.4 (6) |
| **other, % (n)** | 7.1 (1) | 29.4 (5) | 18.8 (6) |
| **Relapse** | | | |
| **local** | 35.7 (5) | 58.8 (10) | 48.4 (15) |
| **metastatic** | 50.0 (7) | 52.9 (9) | 51.6 (16) |
| **metastatic sites** | | | |
| **lung, % (n)** | 42.9 (6) | 41.2 (7) | 41.9 (13) |
| **lymphnodes, % (n)** | 21.4 (3) | 17.6 (3) | 19.4 (6) |
| **liver, % (n)** | 7.1 (1) | 11.8 (2) | 9.7 (3) |
| **bone, % (n)** | 7.1 (1) | 11.8 (2) | 9.7 (3) |
| **skin, % (n)** | 7.1 (1) | 5.9 (1) | 6.5 (2) |
| **other, % (n)** | 7.1 (1) | 5.9 (1) | 6.5 (2) |
| **Marker** | | | |
| **TPS≥1%, % (n)** | 57.1 (8) | 47.1 (8) | 51.6 (16) |
| **TPS <1%, % (n)** | 42.9 (6) | 52.9 (9) | 48.4 (15) |
| **OPC P16+ , % (n)** | 20.0 (1) | 16.7 (1) | 18.2 (2) |
| **OPC not evaluable, % (n)** | 0 | 1 | 1 |
| **1st line therapies** | | | |
| **cetuximab + platin, % (n)** | 42.9 (6) | 17.6 (3) | 29.0 (9) |
| **radiochemotherapy, % (n)** | 57.1 (8) | 76.5 (13) | 67.7 (21) |

**Table 2: Treatment-related adverse events with ≥10% overall incidence in randomized pts.**

| | Nivolumab + Ipilimumab n=13 | | | | Docetaxel n=16 | | | |
|---|---|---|---|---|---|---|---|---|
| | any grade | | grade ≥3 | | any grade | | grade ≥3 | |
| **Adverse event** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| Any event | 5 | 38.5% | 2 | 15.4% | 11 | 68.8% | 6 | 37.5% |
| alopecia | 0 | 0,0% | 0 | 0,0% | 6 | 37,5% | 0 | 0,0% |
| fatigue | 2 | 15,4% | 0 | 0,0% | 3 | 18,8% | 0 | 0,0% |
| anaemia | 3 | 23,1% | 2 | 15,4% | 2 | 12,5% | 0 | 0,0% |
| constipation | 3 | 23,1% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| cough | 1 | 7,7% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| dizziness | 1 | 7,7% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| headache | 1 | 7,7% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| conjunctivitis | 0 | 0,0% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| mucosal inflammation | 0 | 0,0% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| neutropenia | 0 | 0,0% | 0 | 0,0% | 2 | 12,5% | 1 | 6,3% |
| pain | 0 | 0,0% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| pyrexia | 0 | 0,0% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| stomatitis | 0 | 0,0% | 0 | 0,0% | 2 | 12,5% | 0 | 0,0% |
| pneumonia | 4 | 30,8% | 2 | 15,4% | 1 | 6,3% | 1 | 6,3% |
| dyspnea | 2 | 15,4% | 0 | 0,0% | 1 | 6,3% | 0 | 0,0% |
| pleural effusion | 2 | 15,4% | 0 | 0,0% | 1 | 6,3% | 0 | 0,0% |
| hypercalcaemia | 2 | 15,4% | 1 | 7,7% | 0 | 0,0% | 0 | 0,0% |
| insomnia | 2 | 15,4% | 0 | 0,0% | 0 | 0,0% | 0 | 0,0% |
| tumor pain | 2 | 15,4% | 1 | 7,7% | 0 | 0,0% | 0 | 0,0% |

**Table 3: Objective response rate in all randomized pts.**

| | NIVO-IPI (n=14) | DOCE (n=17) |
|---|---|---|
| **CR, % (n)** | 0 | 0 |
| **PR, % (n)** | 0 | 17.6% (3) |
| **SD, % (n)** | 21.4% (3) | 29.4% (5) |
| **PD, % (n)** | 57.1% (8) | 17.6% (3) |
| **NE, % (n)** | 21.4% (3) | 35.3% (6) |

**Figure 1: Progression-free-survival**

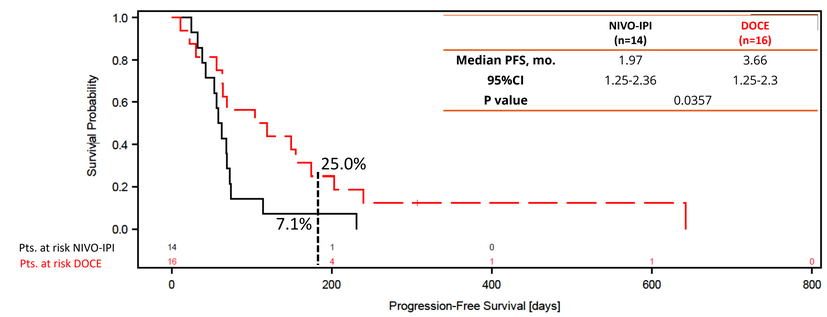



**Figure 2: Overall survival**