News Briefing: Highlights from the 2018 Multidisciplinary Head and Neck Cancers Symposium

Tuesday, February 13, 2018
News Briefing: Highlights from the 2018 Multidisciplinary Head and Neck Cancers Symposium

Moderator: Danielle Margalit, MD, Dana-Farber Cancer Institute

A Randomized, Open-Label, Multicenter, Global Phase 2 Study of Durvalumab (D), Tremelimumab (T), or D Plus T in Patients With PD-L1 Low/Negative Recurrent or Metastatic (R/M) Head and Neck Squamous Cell Carcinoma (HNSCC): CONDOR

  Lillian Siu, MD, Princess Margaret Cancer Centre

Safety evaluation of nivolumab (Nivo) concomitant with platinum-based chemoradiotherapy (CRT) for intermediate (IR) and high-risk (HR) local-regionally advanced head and neck squamous cell carcinoma (HNSCC): RTOG Foundation 3504

  Maura Gillison, MD, PhD, University of Texas MD Anderson Cancer Center

A Phase II Trial of Cabozantinib for the Treatment of Radioiodine (RAI)-refractory Differentiated Thyroid Carcinoma (DTC) in the First-line Setting

  Marcia S. Brose, MD, PhD, Perelman School of Medicine, University of Pennsylvania

OPTIMA—A Phase II Trial of Induction Chemotherapy Response-Stratified RT Dose and Volume De-escalation for HPV+ Oropharynx Cancer: Efficacy, Toxicity, and HPV Subtype Analysis

  Tanguy Seiwert, MD, University of Chicago Medicine
A Phase II Trial of Cabozantinib for the Treatment of Radioiodine (RAI)-refractory Differentiated Thyroid Carcinoma (DTC) in the First-line Setting

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¹University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, ²MD Anderson Cancer Center at Cooper, Camden, NJ, ³NYU School of Medicine, New York, NY, ⁴Johns Hopkins University, Baltimore, MD
Disclosure

• I am employed by the Perelman School of Medicine at the University of Pennsylvania

• I have grant funding from Loxo, Exelixis, Bayer, Eisai, Genzyme/Sanofi, AstraZeneca

• I have received honoraria or consulting fees in the past two years from Eisai, Loxo, Bayer, Genzyme/Sanofi and Blueprint pharmaceuticals
Background

- It is estimated that in the USA in 2017 there were:
  - >56,000 new cases of thyroid cancer, and
  - 2010 deaths due to thyroid cancer

- In approximately 5–15% of patients with thyroid cancer, the disease becomes refractory to radioactive iodine (RAI)

- Median survival for patients with RAI-refractory DTC and distant metastases without additional treatment is estimated to be 2.5–3.5 years

- Patients often suffer multiple complications associated with disease progression

- Two FDA approved agents in the past five years, sorafenib and lenvatinib have shown activity in increasing progression free survival. However, the responses are not durable and toxicities may limit efficacy.

- Additional treatment options are needed for these patients
Background

- Cabozantinib is a multi-tyrosine kinase inhibitor targeting VEGF receptor kinase, RET, MET and AXL
- Cabozantinib is approved for patients with advanced medullary thyroid cancer and renal cell cancer
- Prior data from a phase I study suggested activity in the RAI-refractory DTC patients that had previously been treated with one or more VEGF receptor inhibitors or other therapy in the salvage setting\(^1\)
- In order to further understand the activity of this agent in RAI-refractory DTC, we conducted a single-arm open-label phase II study of cabozantinib in patients in the first-line setting (clinicaltrials.gov: NCT02041260)

\(^1\)Cabanillas et al., Thyroid 2014
UPCC 28313: Cabozantinib for patients with progressive RAI-refractory DTC in the first line setting

Eligibility criteria:
- Metastatic, RAI-refractory thyroid cancer
- No prior treatment with VEGFR inhibitor
- Life expectancy > 3 months
- ECOG PS 0-2
- Good organ and bone marrow function

Primary endpoint:
- Overall Response by RECIST 1.1

Secondary endpoints:
- PFS
- Clinical Benefit Rate
- Safety

n = 35

cabozantinib
60mg daily
Methods

• Between March 2014 and August 2017, 35 patients with metastatic, RAI-refractory, unresectable or locally-advanced thyroid cancer were enrolled on study

• Patients had not received any prior kinase inhibitor therapy

• Starting dose was 60mg PO daily. Dose reductions to 40mg PO daily, then 20mg PO daily and then 20mg PO QOD were allowed

• The agent under study will be deemed of further interest if the response rate is approximately 15% or at least 5 responses out of 35 (CR + PR)
## Patient Characteristics

<table>
<thead>
<tr>
<th>Total Patients</th>
<th>35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>65 years (45-84)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>17 (49%)</td>
</tr>
<tr>
<td>Histology:</td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td>23 (66%)</td>
</tr>
<tr>
<td>Follicular (Hürthle Cell)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Poorly Differentiated</td>
<td>9 (26%)</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th>Best Response (by RECIST 1.1)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>0</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>19 (54%)</td>
</tr>
<tr>
<td>Stable disease (SD)</td>
<td>15 (43%)</td>
</tr>
<tr>
<td>Stable Disease &gt; 6 Months</td>
<td>9 (26%)</td>
</tr>
<tr>
<td><strong>Clinical Benefit Rate</strong></td>
<td><strong>28 (80%)</strong></td>
</tr>
<tr>
<td>(CR+PR+SD&gt;6months)</td>
<td></td>
</tr>
</tbody>
</table>

- **Median Progression Free Survival (PFS)**: Not reached (only 6 PDs thus far)
- **Median Time on Drug**: 35 weeks (3-198)
- **Patients still on Drug as of 2/6/2018**: 16
Results

Best Response per RECIST 1.1
Most Common Treatment Emergent Adverse Events (all grades) as of 2/6/2018

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Hyperglycemia</td>
<td>28 (80%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27 (77%)</td>
</tr>
<tr>
<td>Malaise/Fatigue</td>
<td>26 (74%)</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>25 (71%)</td>
</tr>
</tbody>
</table>
Grade 3-5 Adverse Events (occurring in more than one patient) as of 2/6/2018

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Increased Lipase</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>2 (6%)</td>
</tr>
</tbody>
</table>
Conclusions

• This single site phase II study showed that cabozantinib is an active agent for RAI-refractory DTC in the first line setting
  • Treatment with cabozantinib resulted in a 54% response rate and an 80% clinical benefit rate meeting the primary endpoint of the study (PR+CR >15%)
  • Two kinase inhibitors are currently FDA approved and are used sequentially to improve the progression free interval for these patients, but patients ultimately progress and need more treatment options
  • Cabozantinib was well tolerated with mostly grade 1 and 2 adverse events. No unexpected toxicities were identified
  • Cabozantinib is an active agent in these patients and merits additional study in a large multicenter phase III trial to determine its efficacy in patients with RAI-refractory DTC
Interview Requests and Other Questions

press@astro.org

703-286-1600

On-site Press Office in Scottsdale
Parke Room, Westin Kierland
February 15-16, 8am-4pm MT

A video of the recording will be available following the briefing at
www.astro.org/AMpress