Cauciptabine/Temozolomide chemotherapy in metastatic neuroendocrine tumors - response rate and survival by grade

Katharine Thomas, MS, MD1, Ryan Griffin MD3,4, Brianne A. Voros, MS2,3, J. Philip Boudreaux MD, FACS2,3, Ramcharan Thiagarajan, MD, FACS2,3, Eugene A. Woltering, MD, FACS2,3, Robert A. Ramirez, DO, FACP3,4

1Ochsner Medical Center, Department of Internal Medicine, New Orleans, LA, 2Louisiana State University, Department of Surgery, New Orleans, LA, 3Ochsner Kenner, Neuroendocrine Tumor Clinic, Kenner, LA, 4Ochsner Medical Center, Department of Internal Medicine, Division of Hematology/Oncology, New Orleans, LA

Abstract

INTRODUCTION

• Neuroendocrine tumors (NETs) are commonly treated with various modalities, including surgical, liver-directed, radionuclide, or medical therapy such as chemotherapy.
• The role of chemotherapy has recently evolved. The combination of capecitabine and temozolomide (CAPTEM) has been evaluated in multiple trials and has been shown to have notable activity in grade 1 and 2 pancreatic NETs.
• We present a retrospective study of patients treated with CAPTEM for NETs irrespective of tumor location or grade.

METHODS

• Patients with NETs who received at least one cycle of CAPTEM between June 1, 2012 and May 31, 2018 were included for analysis.
• Data collection included demographics, pathologic characteristics, imaging results, and treatment data.
• Based on the World Health Organization’s classification of NET, grade (G)1 tumors had well differentiated (WD) histology with a ki-67<3, G2 were WD with a ki-67 3-20, G3 were WD with a ki67>20, and NEC were poorly differentiated tumors with ki67>20.
• Response rate was calculated by RECIST 1.1.
• Overall survival (OS) and progression-free survival (PFS) were calculated by the Kaplan-Meier survival method.

RESULTS

This study included 114 patients. Median number of cycles was 9.5. Clinical benefit defined as CR, PR, or stable disease was seen overall in 73.6% and in multiple primary tumor sites including 76% pancreas, 79% small bowel, UPS 66%, 66% colon, 50% lung, 100% kidney. Forty-nine patients died during this period. Median OS was 33 months (CI: 29-44) and median PFS was 12 months (CI:10-23).

Table 1. CAPTEM Response and Survival by Grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>NETs</th>
<th>CAPTEM Response</th>
<th>OS, Overall survival; PFS, Progression free survival. Mo, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low G1</td>
<td>29</td>
<td>Complete 0 (0)</td>
<td>Age at diagnosis Median, years (range) 56 (17-83)</td>
</tr>
<tr>
<td>Median age at diagnosis Median, years (range) 56 (17-83)</td>
<td>12 mo</td>
<td>26 mo</td>
<td>44 mo</td>
</tr>
<tr>
<td>Partial Response, n(%)</td>
<td>17 (59)</td>
<td>4 (22)</td>
<td>6 (33)</td>
</tr>
<tr>
<td>Stable Disease, n (%)</td>
<td>17 (59)</td>
<td>9 (56)</td>
<td>6 (33)</td>
</tr>
<tr>
<td>Progressive Disease, n (%)</td>
<td>10 (34)</td>
<td>7 (44)</td>
<td>8 (44)</td>
</tr>
<tr>
<td>Median PFS</td>
<td>12 mo</td>
<td>12 mo</td>
<td>12 mo</td>
</tr>
<tr>
<td>Median OS</td>
<td>44 mo</td>
<td>44 mo</td>
<td>44 mo</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Clinical benefit was seen using CAPTEM across the spectrum of NETs irrespective of primary site or grade, including neuroendocrine carcinoma. CAPTEM should be considered as a reasonable treatment option for metastatic NETs.
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Abstract
Introduction
Methods
Results 1
Results 2
Conclusion

Please use the headings above to navigate through the different sections of the poster

Methods

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Abstract

Introduction

Methods

Results

Results 1

Results 2

Conclusion

Please use the headings above to navigate through the different sections of the poster

Click to go back to kiosk menu

This study included 114 patients. Median age at diagnosis was 56 years (range: 17-83). Primary tumors included pancreas n=46 (40%), small bowel n=37 (32%), unknown primary site (UPS) n=12 (11%), lung n=12 (11%), colon/rectum n=6 (5%), and kidney n=1(1%). Median number of cycles was 9.5. Clinical benefit defined as CR, PR, or stable disease was seen overall in 73.6% and in multiple primary tumor sites including 76% pancreas, 79% small bowel, UPS 66%, 66% colon, 50% lung, 100% kidney. Forty-nine patients died during this period. Median OS was 33 months (CI: 29-44) and median PFS was 12 months (CI:10-23).

Table 1: Demographics

<table>
<thead>
<tr>
<th>Primary Tumor</th>
<th>N</th>
<th>%</th>
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<tbody>
<tr>
<td>Pancreas</td>
<td>46</td>
<td>40</td>
</tr>
<tr>
<td>GI</td>
<td>43</td>
<td>37</td>
</tr>
<tr>
<td>Lung/Bronchi</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Other Unknown</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: CAPTEM Response and Survival by Grade</th>
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</thead>
<tbody>
<tr>
<td>Low n= 29</td>
</tr>
<tr>
<td>Complete n(%)</td>
</tr>
<tr>
<td>Partial n(%)</td>
</tr>
<tr>
<td>Stable Disease n(%)</td>
</tr>
<tr>
<td>Progressive Disease n(%)</td>
</tr>
<tr>
<td>Median PFS</td>
</tr>
<tr>
<td>Median OS</td>
</tr>
</tbody>
</table>

OS, Overall survival; PFS, Progression free survival; Mo, months

Table 3: CAPTEM response pNET vs non-pNET

<table>
<thead>
<tr>
<th></th>
<th>PNET n=46</th>
<th>Non-PNET n=68</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPTEM Response</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Complete</td>
<td>1</td>
<td>2 0</td>
</tr>
<tr>
<td>Partial</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td>Stable</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td>Progressive</td>
<td>11</td>
<td>24</td>
</tr>
</tbody>
</table>

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Introduction

Methods

Results 1

Results 2

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**Conclusion**

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**References**


