Early CgA response as predictor of outcome following everolimus therapy among patients with low- to intermediate-grade neuroendocrine carcinoma: Analyses of a single institution phase II study

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Abstract

Objectives

The goal of these analyses is to confirm early CgA response as markers of outcome in a single institution phase II study conducted independently of the RADIANT-1 study.

• Assess whether 30% decrease in CgA at week 4 following initiation of everolimus was associated with RECIST response rate, PFS, and OS.

• Assess whether 30% decrease in CgA at week 4 following initiation of everolimus among patients with baseline CgA within normal range was associated with RECIST response rate, PFS, and OS.

Methods

Additional analyses were carried out in our previously published single institution phase II study of octreotide plus everolimus using CgA values collected during the study.

Study design:

Single-arm phase 2 study among patients with metastatic well-differentiated NET (30 carcinoid and 30 islet cell).

• Cohort 1 (N=30): everolimus 5 mg po daily

• Cohort 2 (N=30): everolimus 10 mg po daily

Introduction

Low grade neuroendocrine carcinoma consists of carcinoid, and islet cell carcinoma. Effective systemic therapy options are lacking. While often slow growing, they are nonetheless incurable and lethal when advanced.

We conducted a phase II study of octreotide LAR and everolimus in 60 patients with NETs. A promising intent-to-treat response rate of 20% was observed. Median PFS duration was 60 weeks.

In a follow-up, multi-national phase II study of everolimus in advanced carcinoid, 160 patients were treated in 2 strata, with everolimus (N=115) or octreotide (N=45) plus octreotide based on whether patients were on octreotide at study entry. The median PFS for patients receiving everolimus or octreotide plus octreotide was 24 and 19 months, respectively. Earlier biomarker response with either 30% decrease in normalization of CgA or NSE at week 4 correlated with superior PFS.

Results

Overall study results:

Intent to treat response rate was 20%. Per-protocol response rate was 22%. Response and median PFS are included in Table 1.

Per-protocol of RECIST response rates and median PFS durations.

<table>
<thead>
<tr>
<th>Group</th>
<th>Overall</th>
<th>Carcinoid</th>
<th>Islet cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>13 (22%)</td>
<td>9 (17%)</td>
<td>8 (27%)</td>
</tr>
<tr>
<td>SD</td>
<td>42 (70%)</td>
<td>24 (48%)</td>
<td>18 (80%)</td>
</tr>
<tr>
<td>PD</td>
<td>5 (8%)</td>
<td>1 (2%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>PFS (median)</td>
<td>40 wks</td>
<td>36 wks</td>
<td>50 wks</td>
</tr>
<tr>
<td>OS (median)</td>
<td>40 months</td>
<td>21 months</td>
<td>34 months</td>
</tr>
</tbody>
</table>

Additional analyses were carried out in our previously published single institution phase II study of octreotide LAR and everolimus in advanced pancreatic NETs with progression following chemotherapy (RADIANT-1). 160 patients were treated in 2 strata, with everolimus (N=115) or octreotide (N=45) plus octreotide based on whether patients were on octreotide at study entry. The median PFS for patients receiving everolimus or octreotide plus octreotide was 24 and 19 months, respectively. Earlier biomarker response with either 30% decrease in normalization of CgA or NSE at week 4 correlated with superior PFS.

Conclusion

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References

