Enrollment Insights in the Synchronous mRCC Population: an Update From the Ongoing ADAPT* Phase 3 Study Experience

Robert A. Figlin1, Christopher G. Wood2, and the ADAPT Study Group

Department of Medicine, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; Department of Urology, University of Texas MD Anderson Cancer Center, Houston, TX

*ADAPT: Autologous Dendritic Cell Immunotherapy (AGS-003) Plus Standard Treatment of Advanced Renal Cell Carcinoma (Clinical Trial Identifier: NCT01582672)

Background

AGS-003 is an autologous dendritic-cell DCC-based immunotherapy designed to induce a memory T-cell response specific to a patient’s tumor antigens. Sunitinib is a TKI and standard first-line therapy for metastatic RCC (mRCC), which has been shown to downregulate the immune suppression observed in mRCC.1 In an open-label phase 2 study, AGS-003 plus sunitinib yielded a median overall survival (OS) of over 30 months, in newly diagnosed, unfavorable risk mRCC patients.2 The ADAPT study is a randomized (2:1), international phase 3 study comparing standard targeted therapy + AGS-003 in patients with newly diagnosed, unfavorable risk mRCC.3 The primary objective is to compare the median OS between treatment arms.

AGS-003 Mechanism of Action

• Provides all 3 signals required to generate an adaptive immune response
• These signals stimulate the production of effector memory cytotoxic T lymphocytes (CTLs)
• Memory T-cell responses completely dependent on L-12 secretion by DCs

AGS-003 Production

• RNA encoding full RCC antigen payload (including mutated antigens) isolated and amplified from small tumor specimens collected during nephrectomy (Nx)
• Monocytes isolated from a single leukapheresis are matured into DCs, electroporated with autologous amplified tumor RNA and synthetic CD40L mRNA, then vialed and frozen prior to intradermal administration
• Single production run can deliver multiple years of AGS-003 treatment

Key Eligibility Criteria

• Adults with newly diagnosed mRCC and predominantly clear cell histology
• Metastatic (measurable or non-measurable) disease that can be monitored per RECIST 1.1
• Subjects who are good candidates for cytoreductive Nx follow by standard targeted drug therapy, initiating with sunitinib
• Karnofsky performance status (KPS) ≥70% after recovery from Nx
• Adequate hematologic, renal, and hepatic function
• Life expectancy of 6 months or greater following Nx
• Adequate hematologic, renal, and hepatic function
• No evidence of brain metastases

Eligibility Failures

A total of 180 subjects underwent surgery and tumor collection have been screened and determined to be ineligible for the treatment phase of the study, for the following reasons:
• Non-clear cell (NCC) histology: 72 (40%)
• Lack of measurable or evaluable metastatic disease after Nx: 22 (12%)
• Cardio: History: 15 (8%)
• Investigator decision: 12 (7%)
• Withdrew consent: 9 (5%)
• Other/Not yet specified: 28 (15%)

Percentages of 180 screen failures to date

Eligibility Failures

• Presence of T-regulatory cells
• Prior exposure to therapy: pembrolizumab
• Presence of an active cardiac condition

Study Progress

Primary Endpoint

To compare OS in subjects treated with AGS-003 in combination with standard targeted drug therapy (Arm A) versus standard targeted drug therapy alone (Arm B)

Additional Endpoints

• To compare progression-free survival (PFS) using RECIST 1.1 between study arms

For subjects randomized to treatment May through July 2012:

Arm A

AGS-003 (8 Doses) + Standard Therapy*

for 48 Weeks (N=300)

Arm B

Standard Therapy*

Eligibility Failures

• >130 subjects enrolled and randomized to the treatment phase of the study
• >400 newly diagnosed, mRCC subjects screened and consented for surgery and tumor collection
• >120 active global sites (US, Canada, Spain, Italy, UK, Czech Republic, Israel)

Study Endpoints

For randomized subjects: to compare:

• Safety between study arms
• Objective tumor responses based on RECIST 1.1 between study arms
• Progression-free survival (PFS) using RECIST 1.1 between study arms
• Life expectancy of 6 months or greater following Nx

• Overall, approximately 11%-20% of newly diagnosed, synchronous mRCC patients do not appear to be ideal candidates for standard targeted drug therapy, due to co-morbidities, performance status and/or poor prognosis

• To address the eligibility challenges and screen failure rates observed to date, additional countries and sites have been added to support enrolment completion by end of 2014

• Future study updates will occur during key conferences in late 2014 including the 13th Annual Kidney Cancer Symposium (Oct 2014; Chicago, IL) and SUO 2014 Winter Meeting (Dec 2014; Bethesda, MD)

References


Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Median Age (range, 25–83 y)</th>
<th>Male 75%</th>
<th>T4 10%</th>
<th>G4 44%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Site</td>
<td>59 y (46-83 y)</td>
<td>17%</td>
<td>12%</td>
<td>41%</td>
</tr>
<tr>
<td>Eligibility Failures</td>
<td>T1 7%</td>
<td>T2 14%</td>
<td>T3 66%</td>
<td>G2 12%</td>
</tr>
<tr>
<td>Gender</td>
<td>G1 1%</td>
<td>G3 43%</td>
<td>G4 44%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Summary

• A higher than expected percentage (20%-25% of fully screened subjects) of synchronous mRCC patients have presented with NCC histology

• Overall, approximately 11%-20% of newly diagnosed, synchronous mRCC patients do not appear to be ideal candidates for standard targeted drug therapy, due to co-morbidities, performance status and/or poor prognosis

• To address the eligibility challenges and screen failure rates observed to date, additional countries and sites have been added to support enrolment completion by end of 2014

• Future study updates will occur during key conferences in late 2014 including the 13th Annual Kidney Cancer Symposium (Oct 2014; Chicago, IL) and SUO 2014 Winter Meeting (Dec 2014; Bethesda, MD)

Future presentation at the 50th Annual Meeting of the American Society of Clinical Oncology; May 30-June 3, 2014; Chicago, Illinois.