



Alliance A091802: Phase II Randomized Trial of Avelumab Plus Cetuximab Versus Avelumab Alone in Advanced Cutaneous Squamous Cell Carcinoma of the Skin (cSCC)

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Cutaneous squamous cell carcinoma (cSCC) is one of the most common cancers with an estimated 700,000 new cases diagnosed each year in the United States. [1, 2] While most will have an excellent prognosis, as many as 12,572 patients per year have nodal metastasis and the number of deaths from cSCC per year in the USA is upwards of 8,791, which approaches the annual melanoma-related deaths per year. [2, 3] For patients with locally advanced cSCC without a surgical option or metastatic disease, systemic treatment options are limited. There is limited data with predominantly case series with various chemotherapy agents used for squamous cell carcinomas of other sites. [4] Prospective trials have been conducted with anti-EGFR monoclonal antibodies as well as tyrosine kinase inhibitors in advanced disease. Cetuximab showed a RR of 27% and DCR of 70% however duration of activity was very short with a median PFS and OS of 4 and 8 months respectively. [5] Gefitinib was tested in advanced disease with zero responses and DCR of 27%. [6] More recently, a prospective trial was conducted with anti PD-1 mAb cemiplimab in 59 patients with advanced cSCC. Treatment with cemiplimab led to a RR of 47%, and a 12 month PFS and OS of 52.5% and 80.6% respectively. [7] This led to the approval by the FDA of cemiplimab for the treatment of metastatic cSCC or locally advanced cSCC who are not candidates for curative surgery or curative radiation.

There is a significant rationale for the use of avelumab including in combination with cetuximab in this patient population. This trial will importantly evaluate the safety and efficacy of this combination in advanced cSCC and will be an important step in improving outcomes in this patient population.

References

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Primary

- To evaluate whether treatment with avelumab plus cetuximab prolongs progression free survival (PFS) compared to avelumab alone.

Secondary

- To evaluate the confirmed objective response rate of each treatment arm.
- To evaluate the clinical benefit rate of each treatment arm.
- To evaluate the PFS of cetuximab plus avelumab in patients that have progressed on single agent avelumab.
- To evaluate the overall survival (OS) for each treatment arm.
- To evaluate toxicity across treatment arms of avelumab plus cetuximab and avelumab alone.

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Study Schema



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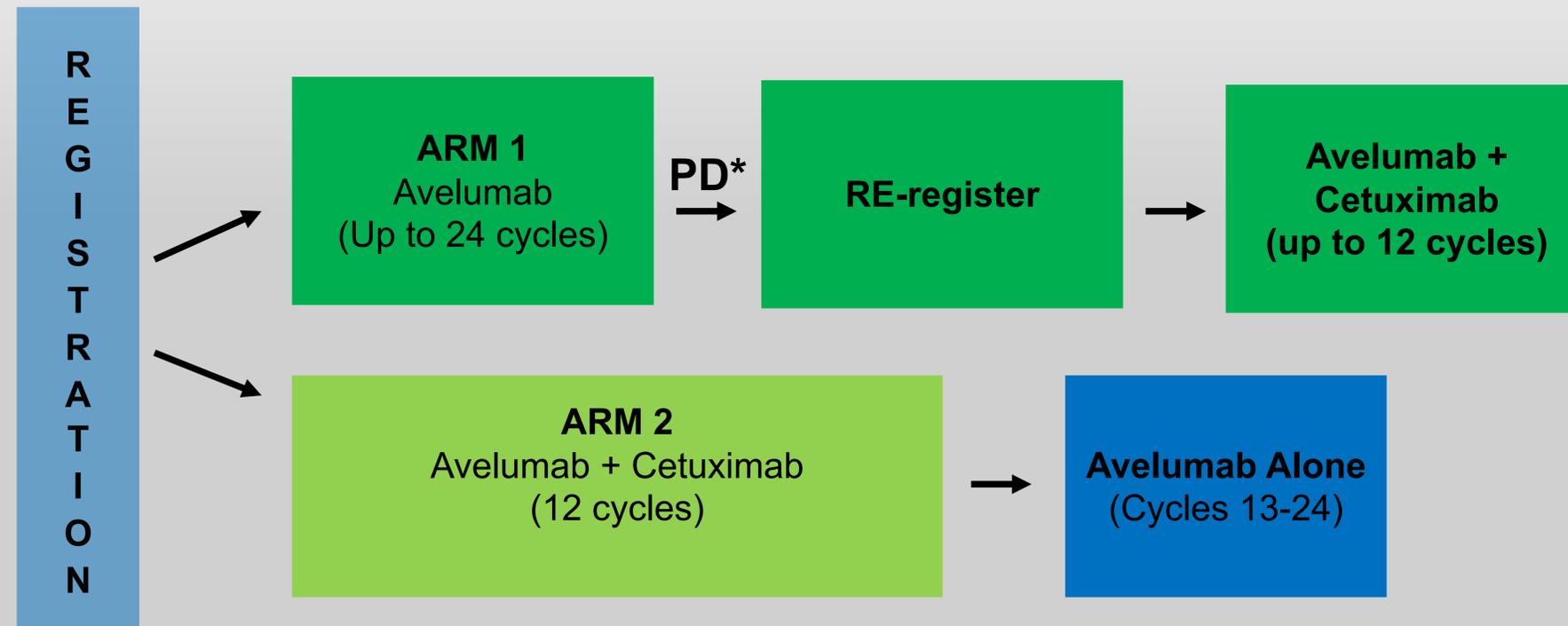
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Treatment is to continue until disease progression or unacceptable adverse event or until the end of the 24 cycle treatment period, whichever comes first. After patients end active treatment, they will be followed for an additional 2 years or until death, whichever comes first.

*Patients that are randomized to avelumab alone and progress will then continue on avelumab with the addition of cetuximab for up to 12 additional cycles or 24 cycles total (including prior cycles of avelumab), whichever occurs first.



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NCI National Clinical
Trials Network

a National Cancer Institute program

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Patients are randomized to 1 of 2 arms.

ARM I

Patients receive avelumab intravenously (IV) over 60 minutes on days 1 and 15. Treatment repeats every 28 days for up to 24 cycles in the absence of disease progression or unacceptable toxicity. Patients with avelumab failure will crossover to arm

ARM II

Patients receive cetuximab IV over 1-2 hours on days 1, 8, 15, and 22 and avelumab IV over 60 minutes on days 1 and 15. Treatment repeats every 28 days for up to 12 cycles for cetuximab and 24 cycles for avelumab in the absence of disease progression or unacceptable toxicity. After completion of study treatment, patients are followed up every 3 months until disease progression, then every 6 months for up to 2 years.

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Pre-Registration Eligibility Criteria

- Provide adequate tissue for PD-L1 testing

Registration Eligibility Criteria

- Biopsy proven advanced cutaneous squamous cell carcinoma.
- Measurable disease
- Patients who received prior treatment with cetuximab as palliative treatment for advanced cSCC are excluded.
- Patients that received cetuximab based chemoradiation as prior treatment for locally advanced disease are eligible as long as the last dosage was given >6 months prior to registration.
- Patients who received cetuximab as part of definitive therapy in the adjuvant setting are eligible as long as the last dosage was given > 6 months prior to registration.
- Patients who received prior cetuximab and had a severe infusion reaction requiring discontinuation of cetuximab are excluded.
- No prior treatment with anti-PD-1 or anti PD-L1 mAbs
- Patients cannot have received treatment with radiation or chemotherapy including another investigational agent within 2 weeks of registration. Other than as stated above for cetuximab there are no limits on the number of lines of other therapies given for advanced cSCC. If patient received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting therapy.
- If patient received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting therapy.
- Not pregnant and not nursing
- Age \geq 18
- ECOG Performance status 0-2

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