agenusnews

Vol. 3 Issue 08 · Apr 21, 2020

Agenus' Bali/Zali Combination in Advanced Cervical Cancer

Durable (12 month follow up), Objective Response Rate of ~26% in patients in a Phase II trial

Advanced cervical cancer is a horrifying disease particularly for young women who come from poor backgrounds and have limited health care coverage. This year more than 14,000 women will be diagnosed with cervical cancer in the US and more than 4,000 women will die. A recent article in the New Yorker profiled the growing prevalence of cervical cancer in states like Alabama, where resources to vaccinate and screen women are lacking[1].

Newly diagnosed patients receive chemotherapy, which has high toxicity and limited activity; the majority of patients relapse in as ealy as six months or less[2]. Adding bevacizumab (a VEGF inhibitor), another approved treatment, marginally improves time to tumor recurrence, but leads to other difficult side effects, like fistulas[3]. Following recurrence, the three other drugs approved for use in cervical cancer have limited activity **(see Table 1)**, with patients relapsing in 2-3 months[4] on average.

Currently available treatments in cervical cancer are ineffective, and seriously compromise the quality of life of patients. **Agenus is committed to changing this reality.**

Data from cervical cancer clinical trials with Agenus' "bali/zali"(PD-1 and CTLA-4 antibodies) have shown a near doubling of response rates, with clinical responses in 14 of the first 55 patients, with a median follow up of ~12 months. We continue to see compelling objective responses in additional patients beyond our previously presented interim analysis data set. This combination therapy has also delivered improved safety as compared to the standard of care chemotherapy, where high grade treatment related adverse events can occur in as many as ~68% of patients[5]. On April 7, 2020 and March 12, 2020, we announced receipt of FDA Fast Track Designation for the investigation of treatment of advanced cervical cancer with our "bali" monotherapy and "bali/zali" combination, respectively.

With additional follow up, an interim analysis of balstilimab monotherapy showed improved response rates of 14.3% (1 CR, 5 PR) in all patients, regardless of PD-L1 biomarker status, and including both squamous cell and adenocarcinoma patients.

Note that Keytruda® was approved by the FDA with ~14% response rate in PD-L1 positive patients, with ~92% of patients having squamous cell histology[4]– these patients generally show better response rates than non PD-L1 positive patients.

Zalifrelimab & balstilimab combination therapy, dosed in a similar patient population, but also includes patients with adenocarcinoma (patients with poorer prognosis) in a Phase II clinical trial, has an estimated ORR of ~26% after ~12 months of follow up (see Table 1). What is most exciting is that these responses are durable in some cases beyond a year; we are optimistic that if these trends continue, we may see certain patients effectively cured.

Table 1. Balstilimab +/- zalifrelimab activity vs. currently available agents in 2L+ cervical cancer

	Chemotherapy Topotecan[5]	Roche Bevacizumab[6]	Merck Pembrolizumab[4]	**AGEN PD1 Balstilimab**	**AGEN - PD1 plus CTLA4 Bali/Zali**
Response rate	**12.5%**	**10.9%**	**14.3%** (PD-L1 positive only)	**14.3%** (all-comers)	**~26%** (all-comers)
Complete response	2.5%	0%	2.6%	**2.4%**	**7.3%**
Partial response	10%	10.9%	11.7%	**11.9%**	**18.2%**

~2X more patients than previously reported.

~2x more active than available treatments

What this data speaks to is that, while PD-1 is the backbone of cancer immunotherapies, the addition of CTLA-4 seems to deliver the "combo push" to make these responses potentially curative. **To this end, we are seeing three-fold higher complete responses in our "bali/zali" combination therapy as compared to currently marketed therapies (Table 1).**

Our goal is to make these effective therapies accessible to patients in need, regardless of where they live or what insurance coverage they have.

References

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