INTERVIEW

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Tracks 1-11

Track 1 Activity of immune checkpoint inhibitors in relapsed/refractory Hodgkin lymphoma (HL)

Track 2 Evaluation of checkpoint inhibitor-based combination regimens for hematologic and solid cancers

Track 3 Predicting response to anti-PD-1 antibodies in patients with advanced HL

Track 4 Activity of nivolumab and pembrolizumab in advanced HL

Track 5 Investigating PD-L1 blockade in HL

Track 6 Consideration of immune checkpoint blockade for patients with advanced HL and prior autoimmune disease

Track 7 Integration of nivolumab into the clinical algorithm for advanced HL

Track 8 Perspective on the use of brentuximab vedotin in clinical practice

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Track 10 Initial therapy options for elderly patients with HL

Track 11 **Case discussion:** A patient with relapsed/refractory HL receives nivolumab on a clinical trial

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Tracks 1, 4 and 7

DR LOVE: Would you comment on the biological basis for the activity of checkpoint inhibitors in Hodgkin lymphoma (HL) and also discuss the available data with nivolumab compared to those with pembrolizumab?

DR ARMAND: Classical HL almost always has a genetic deregulation on the short arm of chromosome 9, and the targets of that deregulation event are the PD-1 ligands, PD-L1 and PD-L2. It's a unique story of biology driving responses, so we have a strong reason to believe that HL might be uniquely susceptible to PD-1 blockade.

Nivolumab and pembrolizumab have been neck and neck, although the development of nivolumab for classical HL preceded that of pembrolizumab. The Phase I data with nivolumab came out a little earlier, and thus we know more about the durability of responses to it. In addition, the patient populations are slightly different in the Phase II trials evaluating these 2 agents. The CheckMate 205 trial of nivolumab included 3 cohorts of patients who had previously undergone ASCT, which differs from the KEYNOTE-087 trial of pembrolizumab, which contains a cohort of patients who were transplant ineligible.

The results from the CheckMate 205 and CA209-039 trials led to the recent FDA approval of nivolumab for patients with classical HL and disease progression after ASCT and brentuximab vedotin (4.1).

The Phase II KEYNOTE-087 study, which was presented at ASCO 2016, showed response rates with pembrolizumab in the range of 70% to 80% for patients with disease that progressed after ASCT and/or brentuximab vedotin (Chen 2016; [4.2]). These results, along with the results of the Phase Ib KEYNOTE-013 study (Armand 2016), led to the FDA breakthrough therapy designation for pembrolizumab in classical HL.

As I mentioned, the KEYNOTE-087 trial also included a cohort of transplant-ineligible patients, and the results indicated that pembrolizumab seems to be as effective in this population as in the post-transplant population. I imagine similar types of approval will be granted, although the labels could be slightly different because of the differences between patient populations on the trials.

DR LOVE: How would you like to use nivolumab now that it is approved for relapsed/refractory HL?

DR ARMAND: It would be nice to use the agent according to the label because otherwise we have little to offer patients in that setting. It is by far the best therapeutic option we have currently, the only drug that rivals nivolumab in HL being brentuximab vedotin, which these patients have already received.

However, nivolumab represents a powerful new therapeutic strategy that we want to use to cure the disease, not necessarily to administer to patients whose disease has

4.1

Efficacy and Safety of Nivolumab for Relapsed/Refractory Classical Hodgkin Lymphoma

Efficacy	Phase I CA209-039 study[1] (n = 23)	Phase II CheckMate 205 study[2] (n = 80)
Objective response rate	87%	66%
Complete response	22%	9%
Partial response	65%	58%
Median PFS	Not reached	10 mo
Overall survival rate	83% (1.5 y)	99% (6 mo)
Select adverse events (any grade)	n = 23	n = 80
Fatigue	NR	25%
Skin related	22%	16%
Hepatic	12%	14%
Pulmonary	4%	2%
Diarrhea	13%	10%
Hypersensitivity/infusion reactions	9%	21%

PFS = progression-free survival; NR = not reported

[1] Ansell S et al. *Proc ASH* 2015;**Abstract 583**; [2] Younes A et al. *Lancet Oncol* 2016;17(9):1283-94.

4.2 **Best Overall Response Rates with Pembrolizumab for Relapsed/Refractory Classical Hodgkin Lymphoma: Results from the Phase II KEYNOTE-087 Study**

Efficacy	Patients with PD after ASCT and BV (n = 30)	Transplant-ineligible patients (n = 30)	Patients with PD after ASCT (n = 30)	Patients with primary refractory disease (n = 37)
Overall response rate	73%	83%	73%	78%
Complete remission	27%	30%	30%	35%
Partial remission	47%	53%	43%	43%
Stable disease	17%	7%	13%	11%
PD	10%	7%	13%	8%
Select adverse events (any grade)	n = 90			
Pyrexia	13%			
Diarrhea	10%			
Neutropenia	8%			
Fatigue	8%			

PD = progressive disease; ASCT = autologous stem cell transplant; BV = brentuximab vedotin

Chen RW et al. *Proc ASCO* 2016;**Abstract 7555**.

already progressed on everything else. So now a whole slew of studies are starting to investigate PD-1 blockade in the first-line salvage setting. We are also conducting a study of PD-1 blockade after ASCT. All the previous steps at which one could potentially position this kind of treatment are being explored.

DR LOVE: Have you tried to access nivolumab for a patient who has not undergone ASCT?

DR ARMAND: We've had the good fortune to participate in various clinical trials, so we haven't run up against not being able to obtain access to nivolumab, but we have used it off label in other settings, such as mediastinal lymphoma, and we also used PD-1 blockade off label prior to its FDA approval.

Another setting of interest is after allogeneic stem cell transplant, which is certainly off label. Some of the results in that setting have been publicly reported in case series, and this is another desperate situation in which people have had success obtaining access to both nivolumab and pembrolizumab. ■

SELECT PUBLICATIONS

Ansell S et al. **Nivolumab in patients (pts) with relapsed or refractory classical Hodgkin lymphoma (R/R cHL): Clinical outcomes from extended follow-up of a phase 1 study (CA209-039).** *Proc ASH* 2015;**Abstract 583**.

Armand P et al. **Programmed death-1 blockade with pembrolizumab in patients with classical Hodgkin lymphoma after brentuximab vedotin failure.** *J Clin Oncol* 2016;[Epub ahead of print].

Chen RW et al. **Pembrolizumab for relapsed/refractory classical Hodgkin lymphoma (R/R cHL): Phase 2 KEYNOTE-087 study.** *Proc ASCO* 2016;**Abstract 7555**.

Younes A et al. **Checkmate 205: Nivolumab (nivo) in classical Hodgkin lymphoma (cHL) after autologous stem cell transplant (ASCT) and brentuximab vedotin (BV) — A phase 2 study.** *Proc ASCO* 2016;**Abstract 7535**.