INTERVIEW

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Tracks 1-5

Select Excerpts from the Interview

Track 1

DR LOVE: Would you discuss the efficacy of the recently FDA-approved anti-EGFR antibody necitumumab in combination with chemotherapy for advanced SCC?

DR RECK: Necitumumab is a human monoclonal antibody directed against EGFR, and it has been investigated in combination with cisplatin/gemcitabine and compared to cisplatin/gemcitabine alone as first-line therapy in the large, randomized Phase III SQUIRE trial for patients with advanced SCC (Thatcher 2015; [4.1]). The trial was positive. The primary endpoint was OS, and we observed a significant improvement favoring the combination of cisplatin/gemcitabine and necitumumab. We also observed an improvement in PFS, although it was marginal. An important question is whether these findings are clinically relevant.

DR LOVE: Do you believe the necitumumab/gemcitabine/cisplatin combination is worth using?

DR RECK: Yes. I believe that currently we have limited treatment options in the first-line setting for patients with SCC, so everything that contributes to an improvement in outcome for the patient is welcome. I would use it, but we must recognize the tolerability and the cost. All of this of course plays a role in the selection of treatment.

DR LOVE: What kinds of side effects have you observed clinically with necitumumab treatment? Is it similar to cetuximab in that regard?

4.1 **SQUIRE: Results of a Phase III Trial of First-Line Gemcitabine/Cisplatin (Gem/Cis) with or without Necitumumab for Stage IV Squamous Cell Non-Small Cell Lung Cancer**

	Gem/cis + necitumumab (n = 545)	Gem/cis (n = 548)	Hazard ratio	*p*-value
Median OS	11.5 mo	9.9 mo	0.84	0.01
Median PFS	5.7 mo	5.5 mo	0.85	0.020
ORR	31%	29%	—	0.400
Select Grade ≥3 AEs	**Gem/cis + necitumumab** (n = 538)		**Gem/cis** (n = 541)	
Neutropenia	24.0%		27.5%	
Anemia	10.6%		10.9%	
Thrombocytopenia	10.0%		10.0%	
Fatigue	7.2%		7.0%	
Hypomagnesemia	9.0%		1.0%	
Skin rash	7.0%		0.4%	
Venous thromboembolic events	5.0%		2.6%	

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; AEs = adverse events

Thatcher N et al. *Lancet Oncol* 2015;16(7):763-74.

DR RECK: The most significant side effects observed in the Phase III FLEX trial of cetuximab were rash, infusion reaction and an increase in myelotoxicity (Pirker 2009). In the SQUIRE trial, again rash was a predominant adverse event associated with necitumumab (Thatcher 2015; [4.1]). Patients who receive necitumumab avoid some of the side effects associated with cetuximab.

Tracks 4-5

CASE DISCUSSION: A 70-year-old man and smoker with Stage IV SCC

DR RECK: I believe this case is representative of the everyday patient with SCC whom you see in the clinic. The patient was in poor condition and certainly not a candidate for cisplatin-based chemotherapy, so we offered carboplatin/gemcitabine. We added bisphosphonates given that the patient also had bone metastases, and the course went well, more or less, with stable disease and a minor response. The treatment was tolerable for the most part, although he did develop some fatigue and myelotoxicity. He also experienced some thrombocytopenia, so we had to modify the gemcitabine dose.

This is something we see frequently with this kind of disease. I take into account the general performance status of the patient, and if the patient is frail, I'm extremely cautious when considering platinum-based chemotherapy. You must be realistic, weighing potential tolerability issues against the response rates in SCC and the efficacy you may observe with platinum-based chemotherapy.

DR LOVE: How do you counsel a patient like this who develops disease progression? What about an immune checkpoint inhibitor?

DR RECK: This patient experienced a PFS of 3 months, which we see frequently in SCC. At that time nivolumab was not available, so he received 4 cycles of second-line docetaxel, but we could achieve only tumor stabilization.

A checkpoint inhibitor would probably be the next option to discuss with him. Is he a candidate for nivolumab? We must be realistic. The prognosis for patients with squamous cell lung cancer is inferior to that for patients with nonsquamous disease, but we do see improvements, and it's important to consider the opportunities because 30% of our patients present with advanced SCC.

We have put a lot of effort into targeted therapies for SCC, and trials are still ongoing (4.2). We have studied PI3K inhibitors in patients with PI3K alterations and FGF inhibitors in patients with FGF amplification. Overall, signs of limited efficacy have emerged, but I'm not sure whether this will be a breakthrough for patients with SCC like the EGFR TKIs have been in EGFR-mutated tumors. ■

4.2 Select Ongoing Trials for Patients with Metastatic Squamous Cell Carcinoma of the Lung

Targeted therapies				
Trial identifiers	Phase	N	Disease setting	Treatment arms
SWOG-S1400 (NCT02154490)	II/III	10,000	• Recurrent disease • Stage IIIB-IV	• Durvalumab (MEDI4736) • Docetaxel • Taselisib (GDC-0032) • Palbociclib • AZD4547 • Rilotumumab/erlotinib • Erlotinib
CEDAR (NCT02423590)	II	140	• Advanced disease	• Gemcitabine/carboplatin/ apatorsen (OGX-427) • Gemcitabine/carboplatin
NCT02428764	II	37	• Unresectable disease • Stage III	• Nimotuzumab/gemcitabine/ carboplatin → surgery
Immune checkpoint inhibitors				
Trial identifiers	Phase	N	Disease setting	Treatment arms
IMpower 111 (NCT02409355)	III	400	• Chemotherapy-naïve disease • Stage IV	• Atezolizumab (MPDL3280A) • Gemcitabine + carboplatin or cisplatin
IMpower 131 (NCT02367794)	III	1,200	• Chemotherapy-naïve disease • Stage IV	• Atezolizumab/*nab* paclitaxel/ carboplatin • Atezolizumab/paclitaxel/ carboplatin • *Nab* paclitaxel/carboplatin

www.clinicaltrials.gov. Accessed January 2016.

SELECT PUBLICATIONS

Pirker R et al. **Cetuximab plus chemotherapy in patients with advanced non-small-cell lung cancer (FLEX): An open-label randomised phase III trial.** *Lancet* 2009;373(9674):1525-31.

Thatcher N et al. **Necitumumab plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone as first-line therapy in patients with stage IV squamous non-small-cell lung cancer (SQUIRE): An open-label, randomised, controlled phase 3 trial.** *Lancet Oncol* 2015;16(7):763-74.