ASCW Preview Part II—Clinical Science Symposium and Poster Discussion

Most of the abstracts are now available online at http://abstract.asco.org/abst_files/HeadNeck_5500-5601.pdf for those with interest. Below, you will find a summary of the three clinical science symposium abstracts and the poster discussion abstracts. There’s a lot to cover…

**Phase II study of figitumumab in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck: GORTEC 2008-02**

Figitumumab is an antibody that inhibits the insulin-like growth factor receptor. As a single agent, it does not appear to be active in platinum-refractory SCCHN.

**BIBW 2992 versus cetuximab in patients with metastatic or recurrent head and neck cancer (SCCHN) after failure of platinum-containing therapy with a cross-over period for progressing patients: Preliminary results of a randomized, open-label phase II study.**

BIBW2992 is a pill that inhibits both EGFR and HER2. I believe in the potential of inhibiting both EGFR and HER2 enough to have opened a trial of it with a related drug. Response rate here was 18%, at least as good as the 8% seen with cetuximab, reinforcing the idea that this general strategy is worthy of further testing.

**Long-term results in a cohort of medullary thyroid cancer (MTC) patients (pts) in a phase I study of XL184 (BMS 907351), an oral inhibitor of MET, VEGFR2, and RET.**

The maximum tolerated dose in this large phase I study was 175mg daily. There was strong evidence of activity-29% partial response, 4 additional patients with at least 30% shrinkage at some point, and 41% stable disease for at least six months. There were responses in patients with and without RET mutations. A phase III study is ongoing, which seems warranted based on these results.

**Long-term results from TAX324: A phase III trial of sequential therapy comparing TPF to PF in locally advanced (LA) squamous cell cancer of the head and neck (HNC).**

Chemotherapy got its start in head and neck cancer given before radiation (called neoadjuvant or “induction” chemotherapy). We later learned that it was better to give the chemo and radiation at the same time, so concurrent chemoradiation gained favor. A number of trials now look at adding induction chemotherapy before concurrent chemoradiation (so chemo then chemo + radiation together). This trial updates published results comparing two different modalities of induction chemotherapy-cisplatin plus 5-FU vs. cisplatin + 5-FU plus docetaxel. The three drug regimen continues to win with more followup, showing the merits of docetaxel in this therapy. We will newly see data showing that the effect size was bigger in patients > 55 years of age than in younger patients. This could be practice changing for those oncologists.
who use TPF for young patients, but consider it too toxic for older patients. However, the use of induction chemotherapy itself remains unproven and controversial. A trial by this same group aimed to answer the “induction vs. no induction” question. In the general poster session, we will learn that this study closed early, with only 145 patients accrued; based on the abstract, it look like we may see only toxicity, and not efficacy data this year at ASCO. Here at GRACE, we plan to discuss this topic further on an upcoming webinar.

Phase II induction cetuximab (C225), paclitaxel (P), and carboplatin (C) followed by chemoradiation with C225, P, C, and RT 68-72Gy for stage III/IV head and neck squamous cancer: Primary site organ preservation and disease control at 2 years (ECOG, E2303).

The induction theme continues. TAX324 is clearly an important study: it re-raises the induction question in an era of chemoradiotherapy and shows the merits of docetaxel in induction chemotherapy. However, some oncologists, including myself, have criticized the TPF regimen for being too toxic and not feasible. Too many patients have toxicities that stop them from undergoing full definitive-chemorads, the part of the treatment paradigm that is best proven at this point. Many of those who criticize TPF feel that the problem is that 5-FU and cisplatin are too toxic, leading to multiple studies of variants on the regimen. We’ve seen E2303 before at ASCO, where preliminary results looked good, but no survival numbers were presented. Here they are with more followup.

TPF induction-radioimmunochemotherapy for the treatment of advanced head and neck cancer.

This study looked at a lot at once: TPF induction, cisplatin plus cetuximab chemoradiotherapy, neulasta, and PET/CTs. Patients got 3 cycles of TPF, with peg-filgrastim (neulasta) support followed by cisplatin/cetuximab chemoradiation. Neulasta is a medicine that raises white blood cell counts. While its use in head and neck cancer, or any curative-intent therapy, is a bit controversial, it addressed the major problem in TAX324-neutropenia (low levels of a particularly important kind of white blood cell). 8 of 152 patients had to stop therapy after induction chemotherapy-I look forward to learning more about these 8 patients at ASCO. Response rates were good, cisplatin/cetuximab seems promising and the authors feel that PET/CT helped, but I remain most excited to learn about how neulasta affected the feasibility of induction with TPF and to see detailed toxicity and feasibility data.

Induction docetaxel, cisplatin, and cetuximab (TPE) followed by concurrent radiotherapy, cisplatin, and cetuximab and maintenance cetuximab in patients with locoregionally advanced head and neck cancer (HNC): Mature results with HPV analysis.

We’ve seen this study before at ASCO. If 5-FU is the most toxic part of TPF, perhaps substituting the much less toxic cetuximab for it can decrease toxicity, increase feasibility, and improve treatment results. Preliminary results of this phase II study continue to look good. Most interesting, however, is the HPV data. Dr. Jimeno recently addressed HPV on GRACE,
describing the growing data-set showing how much better HPV+ patients do. This study flies in the face of this, showing excellent and similar results for HPV+ and HPV- patients. Is it possible that induction chemotherapy can overcome the negative prognostic effect of HPV negativity?

Radiation alone (RT) versus RT with concomitant chemotherapy (CT) in stages III and IV oropharynx carcinoma: Ten-year results of the 94-01 GORTEC randomized study.

This study is a classic in head and neck cancer. It demonstrated the merits of adding chemotherapy to radiation. This poster updates the results at ten years, showing that they stand up with a doubling of cure rates at 10 years.

Need for postradiotherapy neck dissection by tumor site and nodal stage for head and neck cancer.

After chemoradiotherapy, should patients still have neck dissection (surgical removal of lymph nodes in the neck)? This has been a major debate in SCCHN for a long time that rages on. In this retrospective review, isolated neck failures were similar in number between those who had the surgery and those who didn’t, raising the question of whether the surgery helps or not. Of course, there’s probably a bias here in that this was not a randomized study-patients who got extra treatment probably got it for a good reason. Patients with hypopharyngeal N2 disease with nodes over 3cm had particularly high relapse rates, even when the nodes seemed negative after chemoradiation. The phrasing of the abstract leaves me uncertain that I completely understand the results of this study, so I’m looking forward to seeing the actual poster. Also, I don’t have strong feelings about who should have nodal dissection because I don’t think that the existing data properly answer the question. For this reason, I’m looking forward to hearing the discussant’s views. Finally, consistent with previous reports and common sense, the review shows worse results for those who have residual living cancer cells in the neck dissection after chemorads. I look forward to discussing with my colleagues what should be done with these patients. Do they need more therapy to elicit cure? Or have their cancers proven that they are not sensitive to such therapy, so that it would only cause side effects?

Clinical efficacy and tolerability of continuous course reirradiation with concurrent weekly carboplatin-paclitaxel for locally recurrent, nonmetastatic squamous cell carcinoma of the head and neck (SCCHN).

When SCCHN recurs, it tends to do so locally, rendering recurrence potentially curable by salvage surgery or repeat radiation. This study looks at a new way to do this. In particular, most of the existing data is with hydrea/5-FU chemoradiation, but this study uses the more popular carboplatin/paclitaxel. I hope that the poster shows what kind of therapy the patients got the first time around.

PTEN as prognostic and predictive marker in postoperative radiotherapy for squamous cell cancer of the head and neck.
Radiation is typically given five days per week, with the weekends off. My radiation oncology colleagues have explained to me that radiation simply does not work on the weekends. This study compared five day per week radiation to seven day per week radiation, given after surgery. Patients with high intensity of PTEN staining (a tumor suppressor) gained from 7 day per week radiation, while patients with low PTEN did not. The study suggests that PTEN may serve as a **prognostic** or **predictive** marker in postoperative radiotherapy, and that my radiation friends may eventually have to work a few more weekend days. Of note, none of these patients got chemotherapy with their radiation, and there is reason to believe that altered fractionation of radiation may be less effective when combined with chemotherapy (so if any of my radiation friends are reading this, please note that it may be medical oncologists who rescue your weekends!) (And for those who object to my nerdy, pathetic attempts at humor here, I ask you this: If you can’t joke about immunohistochemical markers predicting the efficacy of altered fractionation regimens in head and neck cancer, what can you joke about?)

**Use of XPF expression in tumors and XPF single nucleotide polymorphisms to predict clinical outcome in head and neck cancer.**

We’ve talked before on GRACE about the potential value of ERCC1 as a tumor marker in lung cancer. This poster looks at treatment responses divided by levels of XPF expression (XPF is a subunit of the ERCC1 endonuclease that protects DNA against damage from radiation and platinum compounds). Lower expressers seemed to have better outcomes, including in the oropharynx subset.

**Gene expression profiling of oral preneoplastic lesions (OPL) from a prospective prevention trial.**

A 21 gene signature may help predict which patients with pre-cancers in their mouth will go on to develop frank cancer.

**Comparison of primary site biopsies and transverse surgical sections of squamous cell carcinoma of the head and neck for translational research analysis.**

When you do a biopsy, you get only a tiny piece of a tumor. Even if all of your tests on that biopsy are perfect, you could only be certain about that exact spot. So, how representative are superficial and core biopsies in SCCHN? For EGFR, neither type of biopsy correlated well with full surgical specimens. For Ki67 (a marker for proliferation), core biopsy did not correlate well, but superficial biopsy did. The implications of this study for translational research are huge—at least for EGFR, we cannot reliably depend on a biopsy as representing the whole tumor.

**Association of circulating tumor cells are associated with lymph node metastasis in squamous cell carcinoma of the head and neck region (SCCHN).**

We’ve talked about circulating tumor cells on GRACE before both in general, and in the context of lung cancer. This study looked at 40 patients with locally advanced SCCHN. They were able to detect circulating tumor cells in 40%. There were fewer CTCs in patients with no lymph nodes involved with cancer or only 1 affected lymph node. In my opinion, CTCs could
Usefulness of interim FDG-PET after induction chemotherapy in patients with locally advanced squamous cell carcinoma of the head and neck receiving induction chemotherapy and definitive chemoradiotherapy.

Uptake on PET and changes in uptake on PET may be helpful in predicting who will have a complete response to treatment. Future studies will be necessary to tell us how we can use this information in treatment decisions.

Oropharynx cancer (OPC) in TAX 324: Human papillomavirus (HPV) and survival.

Updated results from TAX324 will be presented in the oral session. Here, results are divided by HPV status. The results for the HPV+ group are fantastic at 5 years-78% disease free survival! What contributes to this result? Is it just that the HPV+ patients are younger and better able to tolerate the aggressive TPF regimen? Or, is the biology of HPV+ cancer also different, leading to better treatment responses? Can we reduce the intensity of post-induction therapy for the HPV+ patients to improve their long term functional outcomes? Even as I dislike the Cis/5-FU backbone of TPF, it’s hard not to admire how much Dr. Posner, Dr. Haddad and colleagues are driving the field!

A population-based evaluation of incidence trends in oropharynx cancer (OP) focusing on socioeconomic status (SES), sex, and race/ethnicity.

In CA, non-Hispanic white males have an increasing incidence of oropharynx cancers, independent of socioeconomic status.

Human papillomavirus (HPV) transmission from oropharyngeal cancer patients to sexual partners.

The good news about HPV is that prognosis with current modalities of therapy seems better. The bad news is that HPV is transmissible and this study supports the idea that strains that cause cancer really are being transmitted. Could the HPV vaccine eventually help with this problem?

Relationship between epidermal growth factor receptor (EGFR) gene copy number, p16 status, and outcome in locally advanced squamous cell carcinoma of the head and neck (LASCCHN).

EGFR FISH positive has been reported to be a predictor of bad outcomes in SCCHN. HPV (measured by p16) has been reported to be a predictor of good outcomes. It seems that an individual patient is unlikely to have both of these markers at the same time.

Plasma human papillomavirus (HPV) DNA as a potential tool for tumor detection and monitoring response in HPV-related oropharyngeal carcinoma (OP).
This is a basic science study that suggests that we may be able to use HPV DNA in blood to follow therapy. It’s a great idea and I look forward to human data.

An open-label, randomized, study of h-R3mAb (nimotuzumab) in patients with advanced (stage III or IVa) squamous cell carcinoma of head and neck (SCCHN): Four-year survival results from a phase IIb study.

Nimotuzumab plus radiation was better than radiation alone. This antibody has the same target as cetuximab. Because it is fully humanized, it is unlikely to have the same infusion-reaction problem that some parts of the country have with cetuximab.

Phase II trial of the irreversible oral pan-HER inhibitor PF-00299804 (PF) as first-line treatment in recurrent and/or metastatic (RM) squamous cell carcinoma of the head and neck (SCCHN).

EGFR is only one of several members of the HER family. Treatments targeting other members have promise in SCCHN. I’m working on one such trial. This trial gave a pan-HER inhibitor and demonstrated antitumor activity without any cytotoxic IV chemotherapy.

A phase II study of sorafenib in combination with carboplatin and paclitaxel in patients with metastatic or recurrent squamous cell cancer of the head and neck (SCCHN).

This was an early presentation of only 22 patients in a study with planned accrual of 43 patients. Early results are very good, but I think that it’s too early to say much. I’m looking forward to the discussion to better understand why this was accepted to poster discussion at this early stage.

Pemetrexed (P) and bevacizumab (B) in patients (pts) with recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN): Final results and correlation with TS, MTHFR, and VEGF gene polymorphisms.

Response rate was 30% and median overall survival was 11.5 months. Although pemetrexed did not show early promise in treating SCCHN, I am interested in these results. The incurable patient is more heavily pretreated than ever before; because neither of these agents are part of standard curative-intention therapy, they may be new options for these patients.

Is there a role for adjuvant cetuximab after radiotherapy (RT) plus cetuximab in patients (pts) with locally advanced squamous cell carcinoma of the oropharynx? A phase II randomized trial.

Half these patients with oropharyngeal cancer got an extra 12 weeks of cetuximab after cetuximab chemoradiation. At two years of followup, cetuximab may have resulted in a small improvement both in event free survival and overall survival. I look forward to seeing the shape of the curves (did cetuximab simply delay recurrence, or truly result in increased cure?) Also, remember that this is a phase II study; although it was randomized, it’s not a phase III study. It raises an interesting hypothesis, but does not prove it.
Chemoprevention with erlotinib and celecoxib in advanced premalignant lesions of the head and neck: Results of a phase I study.

The only thing better than curing cancer is preventing it. This phase I study looked at erlotinib and celecoxib in patients with pre-cancers. The goal of a phase I study is to find the right dose—here it was erlotinib 75mg daily plus celecoxib 400mg twice per day. Response rates in patients with moderate dysplasia (precancer) or severe dysplasia were good, a total of 71%. A phase II study is planned.

Phase II study and tissue correlative studies of AZD6244 (ARRY-142886) in iodine-131 refractory papillary thyroid carcinoma (IRPTC) and papillary thyroid carcinoma (PTC) with follicular elements.

AZD6244 is a pill that works by targeting MAPK and MEK-1/2. In this study of 39 patients, therapy was well tolerated. While there was only one response, many patients had stable disease and progression free survival was over a year.