INTERVIEW

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Tracks 1-18

Track 1 Results of the SSGXVIII study: Twelve versus 36 months of adjuvant imatinib for operable, high-risk GIST

Track 2 Long-term results from a Phase II study of standard- versus higher-dose imatinib for unresectable or metastatic, KIT-positive GIST

Track 3 **Case 1 discussion:** A 66-year-old woman with abdominal pain has a duodenal mass on CT and undergoes resection for a 3-cm KIT-expressing GIST with a mitotic index of 6 per 50 HPF

Track 4 Duration of adjuvant imatinib treatment for patients with high-risk GIST

Track 5 Sorafenib in advanced GIST

Track 6 **Case 2 discussion:** An otherwise healthy 78-year-old woman with a 4-cm, KIT-positive gastro-esophageal junction (GEJ) GIST refuses surgery

Track 7 **Case 3 discussion:** A 62-year-old man with a 5-cm, moderately differentiated adenocarcinoma of the cecum with negative margins and 0 of 15 positive nodes

Track 8 Role of Onco*type* DX® and other genomic assays in early-stage colon cancer

Track 9 **Case 4 discussion:** A 47-year-old man with an asymptomatic, moderately differentiated adenocarcinoma of the transverse colon and a 4-cm, biopsy-proven hepatic metastasis

Track 10 Perioperative FOLFOX/bevacizumab for patients with synchronous asymptomatic primary colon cancer and resectable hepatic metastases

Track 11 FOLFIRI with or without aflibercept as second-line therapy of metastatic colorectal cancer (mCRC)

Track 12 Influence of K-ras G13D mutations on outcome in patients with mCRC treated with first-line chemotherapy with or without cetuximab

Track 13 Roles of capecitabine and oxaliplatin in chemoradiation therapy for rectal cancer

Track 14 Emerging role of everolimus and sunitinib in the treatment of pancreatic neuroendocrine cancer

Track 15 New approaches to adjuvant therapy for gastric or GEJ cancer

Track 16 Duration of trastuzumab in the treatment of advanced, HER2-positive gastric cancer (GC)

Track 17 Role of sorafenib in advanced hepatocellular carcinoma (HCC)

Track 18 RTOG-9811 study: Radiation therapy with either 5-FU/mitomycin or 5-FU/cisplatin in anal carcinoma

Select Excerpts from the Interview

Tracks 1-2, 5

DR LOVE: What are your thoughts on the SSGXVIII/AIO trial of adjuvant imatinib therapy for patients with operable gastrointestinal stromal tumors (GIST) with a high risk of recurrence?

DR BLANKE: This trial demonstrated a marked improvement in recurrence-free survival for 3 years versus 1 year of treatment, but the surprising observation from this study was the overall survival benefit (Joensuu 2011; [1.1]).

Previous studies, such as the ACOSOG-Z9001 trial, demonstrated a dramatic improvement in recurrence-free survival with 1 year of imatinib therapy but no overall survival benefit (DeMatteo 2009). Unfortunately as a result, some oncologists decided not to treat with adjuvant imatinib because they thought they could catch up at the metastatic stage.

The SSGXVIII/AIO trial provides 3 take-home messages. First, 3 years is the new gold standard for imatinib adjuvant therapy. Second, due to the overall survival benefit, it is no longer practicable to wait for patients to experience relapse. Last, whether adjuvant imatinib therapy is curative or whether it merely prolongs disease remission in these patients is yet to be determined.

This has important implications for determining if 3 years is the actual "magic number" or whether it is 5 or 10 years or whether these patients should undergo lifelong treatment, although this is a huge commitment for a patient who may already have been cured. In practice, I will continue adjuvant imatinib therapy beyond the 3-year treatment point if I can.

1.1

SSGXVIII/AIO: A Randomized Phase III Clinical Trial of 12 versus 36 Months of Adjuvant Imatinib Therapy for Patients with High-Risk Gastrointestinal Stromal Tumors

Outcome	One-year arm (%)	Three-year arm (%)	Hazard ratio	*p*-value
Five-year RFS	47.9	65.6	0.46	<0.0001
Five-year OS	81.7	92.0	0.45	0.019

RFS = recurrence-free survival; OS = overall survival

Joensuu H et al. *Proc ASCO* 2011;**Abstract LBA1**.

DR LOVE: Any other important new studies in the treatment of GIST?

DR BLANKE: I was involved with the B2222 trial that began patient enrollment about 10 years ago (von Mehren 2011). This was a randomized Phase II study of 400 versus 600 milligrams per day of imatinib for patients with KIT-positive, unresectable or metastatic GIST. Though not surprising, an interesting result from this study was a 35% 9-year overall survival rate, meaning

that a third of all patients were alive and well after almost a decade. Of importance is the result that few relapses occurred after about 5 to 6 years. This has important implications for how we survey patients in the future. It negates the need for quarterly or semiannual CTs, thereby resulting in less frequent patient monitoring and reduced exposure to radiation and IV dye.

DR LOVE: What about the role of sorafenib in advanced GIST?

DR BLANKE: Sorafenib is a multikinase inhibitor approved for the treatment of advanced renal cell carcinoma and unresectable hepatocellular carcinoma (HCC) and has also been "floating around" for a while in GIST therapy. Data at ASCO 2011 reported an approximate 70% tumor control rate without disease progression for about 5 months when sorafenib was administered as late-line therapy (Kindler 2011; [1.2]).

Regorafenib, a later derivative of sorafenib, is another modestly promising agent in advanced GIST therapy. It is possible that one of these will eventually be moved up into the adjuvant setting as combination therapy or monotherapy.

1.2

Phase II Consortium Trial of Sorafenib for Patients with Imatinib (IM)- and Sunitinib (SU)-Resistant Gastrointestinal Stromal Tumors

	IM resistant (n = 6)	**IM/SU resistant** (n = 32)
Partial response	17%	13%
Stable disease	50%	56%
Disease control rate	67%	69%

Kindler HL et al. *Proc ASCO* 2011;**Abstract 10009**.

Tracks 15-16

DR LOVE: Anything presented at ASCO 2011 in gastric cancer (GC) that caught your attention?

DR BLANKE: Because intensifying cancer therapy in the metastatic GC setting may yield better outcomes, particularly with the addition of an anthracycline, in the CALGB-80101 adjuvant trial for patients with gastric or gastroesophageal junction adenocarcinoma 5-FU was administered during radiation therapy but then intensified systemically with epirubicin/cisplatin/5-FU (Fuchs 2011). The trial was slow to accrue and it was "stone cold negative" without a hint of benefit. Hence, 5-FU adjuvant therapy remains the standard used with radiation therapy in North America.

The Phase III CLASSIC trial, which evaluated capecitabine/oxaliplatin without radiation therapy for GC, reported a dramatic improvement in disease-free survival (Bang 2011). Although improvement has not yet been observed in overall survival, that may occur in time as a trend emerged toward statistical significance with a *p*-value of 0.0775.

DR LOVE: Have we seen new developments in advanced GC with regard to anti-HER2 treatment?

DR BLANKE: I consider HER2 testing to be a new standard procedure in GC. The ToGA trial results in advanced GC mandate trastuzumab treatment for patients with HER2-positive GC (Bang 2010; [1.3]). Considering it is being used in the metastatic setting, I will certainly treat with trastuzumab until disease progression. Unlike breast cancer, treatment with trastuzumab beyond disease progression in GC has garnered little enthusiasm, although this may be the right approach to take. ■

1.3

ToGA: Efficacy from a Phase III Study of the Addition of Trastuzumab to First-Line Chemotherapy for HER2-Positive Advanced Gastric or Gastroesophageal Junction Cancer

Efficacy	FC (n = 290)	FC + T (n = 294)	Hazard ratio	*p*-value
Median overall survival	11.1 mo	13.8 mo	0.74	0.0046
Median progression-free survival	5.5 mo	6.7 mo	0.71	0.0002
Overall response rate	35%	47%	—	0.0017
Duration of response	4.8 mo	6.9 mo	0.54	<0.0001

F = fluoropyrimidine (5-FU or capecitabine); C = cisplatin; T = trastuzumab

Bang YJ et al. *Lancet* 2010;376(9742):687-97.

SELECT PUBLICATIONS

Bang YJ et al. **Adjuvant capecitabine and oxaliplatin for gastric cancer: Results of the phase III CLASSIC trial.** *Proc ASCO* 2011;**Abstract LBA4002**.

Bang YJ et al. **Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): A phase 3, open-label, randomised controlled trial.** *Lancet* 2010;376(9742):687-97.

DeMatteo RP et al. **Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: A randomised, double-blind, placebo-controlled trial.** *Lancet* 2009;373(9669):1097-104.

Fuchs CS et al. **Postoperative adjuvant chemoradiation for gastric or gastroesophageal junction (GEJ) adenocarcinoma using epirubicin, cisplatin, and infusional (CI) 5-FU (ECF) before and after CI 5-FU and radiotherapy (CRT) compared with bolus 5-FU/LV before and after CRT: Intergroup trial CALGB 80101.** *Proc ASCO* 2011;**Abstract 4003**.

Joensuu H et al. **Twelve versus 36 months of adjuvant imatinib (IM) as treatment of operable GIST with a high risk of recurrence: Final results of a randomized trial (SSGXVIII/AIO).** *Proc ASCO* 2011;**Abstract LBA1**.

Kindler HL et al. **Sorafenib (SOR) in patients (pts) with imatinib (IM) and sunitinib (SU)-resistant (RES) gastrointestinal stromal tumors (GIST): Final results of a University of Chicago Phase II Consortium trial.** *Proc ASCO* 2011;**Abstract 10009**.

Von Mehren M et al. **Follow-up after 9 years (yrs) of ongoing, phase II B2222 trial of imatinib mesylate (IM) in patients (pts) with metastatic or unresectable KIT+ gastrointestinal stromal tumors (GIST).** *Proc ASCO* 2011;**Abstract 10016**.