Circulating tumor cells in newly diagnosed inflammatory breast cancer.


Introduction: Circulating tumor cells (CTCs) are an independent prognostic factor for progression-free survival (PFS) and overall survival (OS) in patients with metastatic breast cancer. Inflammatory breast cancer (IBC) is one of the most aggressive forms of breast cancer. The prognostic value of a CTC count in newly diagnosed IBC has not been established. The aim of this study was to assess the prognostic value of a baseline CTC count in patients with newly diagnosed IBC.

Methods: This retrospective study included 147 patients with newly diagnosed IBC (77 with locally advanced and 70 with metastatic IBC) treated with neoadjuvant therapy or first-line chemotherapy during the period from January 2004 through December 2012 at The University of Texas MD Anderson Cancer Center. CTCs were detected and enumerated using the Cell Search system before surgery alone.

Results: The proportion of patients with 1 CTC was lower among patients with stage III than among patients with metastatic IBC (54.5% versus 84.3%; P=0.0002); the proportion of patients with 5 CTCs was also lower for stage III than for metastatic IBC (19.5% versus 47.1%; P=0.0004). Patients with <5 CTCs had significantly better progression-free survival (PFS) (hazard ratio [HR]=0.60, P=0.02) and overall survival (HR=0.59, P=0.03) than patients with 5 CTCs. Among patients with stage III IBC, there was no significant difference in PFS (HR=0.66, 95% confidence interval [CI], 0.31 to 1.39; P=0.29) and OS (HR=0.54, 95% CI, 0.24 to 1.26; P=0.48) in patients with no CTCs compared to patients with 1 CTC. In multivariate analysis, CTC was prognostic for PFS and OS independently from clinical stage.

Conclusions: CTCs can be detected in a large proportion of patients with newly diagnosed IBC and are a strong predictor of worse prognosis in patients with newly diagnosed IBC.

Mego M
Emerging role of circulating tumor cells in cancer management. (Editorial)

Circulating tumor cells (CTCs) play a crucial role in metastatic cascade, tumor dissemination and progression. CTCs represent a unique biomarker and are different from any of existing cancer biomarkers, as they represent a sampling of a patient’s tumor. Prognostic value of CTCs was demonstrated in numerous clinical trials in primary and metastatic breast cancer patients. Several trials are ongoing aimed to demonstrate clinical utility of CTCs detection and profiling to facilitate rational treatment decisions for breast cancer patients.

SARKÓMY
KIT and PDGFRA Mutations and the Risk of GI Stromal Tumor Recurrence.

Purpose: Mutated KIT and platelet-derived growth factor alpha gene (PDGFRA) drive GI stromal tumor (GIST) oncogenesis, but the clinical significance of their single mutations is known incompletely.

Patients and methods: We identified 11 population-based series of patients with GIST through a literature search and pooled individual data from 3,067 patients treated with macroscopically complete tumor excision. Mutation analysis was done from 1,505 tumors. We analyzed associations between KIT and PDGFRA mutations and recurrence-free survival (RFS) in the subsets in which patients were treated with surgery alone.

Results: We identified 301 different single mutations in KIT and 33 in PDGFRA. Patients with PDGFRA mutations had more favorable RFS than those with KIT mutations (hazard ratio, 0.34; P=.004). Only one of the 35 GISTs with KIT exon 11 duplication mutations recurred. Patients with deletions of only one codon of KIT exon 11 had better RFS than those with another deletion type, and some KIT exon 11 substitution mutations (Trp557Arg, Val559Ala, and Leu576Pro) were also associated with favorable RFS. Patients with an identical mutation had greatly variable outcomes depending on the standard prognostic factors, notably, mitotic count. Commonly used risk stratification schemes tended to overestimate the risk for recurrence in subgroups with prognostically favorable mutations.

Conclusion: GISTs with an identical KIT or PDGFRA mutation may have widely varying risks for recurrence. Most of the patients with PDGFRA mutations and hose with KIT exon 11 duplication mutation or deletion of one codon have favorable RFS with surgery alone and are usually not candidates for adjuvant therapy.

GENITOURINÁRNE MALIGNITY
Vrdoljak E, Gécz I, Mardiaj K, Cselefan TE, Leyman S, Zhang K, Sajben P, Torday L.
Central and Eastern European Experience with Sunitinib in Metastatic Renal Cell Carcinoma: A Sub-analysis of the Global Expanded-Access Trial.
Pathol Oncol Res. 2015 Jan 4. [Epub ahead of print]

A global, open-label, expanded-access trial (EAT) provided sunitinib treatment on a compassionate-use basis to patients with metastatic renal cell carcinoma (mRCC) between 2005 and 2011. This retrospective analysis examines outcomes in patients from Central and East European (CEE) countries participating in the global EAT. Sunitinib (starting dose 50 mg orally once daily, with dose reduction for toxicity) was administered in repeated 6-week cycles (4 weeks on and 2 weeks off) until occurrence of disease progression or unacceptable to-
or intravenous bleomycin [30 mg per day on days 1, [100 mg/m(2) per day for 5 days], and intramuscular 

prognosis criteria. After one cycle of BEP (intravenous 
International Germ Cell Cancer Consensus Group poor 

treatment intensification reduces the risk of 
were only cured in about half of patients. We 

aimed to assess whether treatment intensification 

mRCC patients in CEE countries. Expanded-access program patients 

showed a lower tumor response rate but similar 

survival outcomes to patients in the pivotal Phase 
III clinical trial of sunitinib in mRCC.


Personalised chemotherapy based on tumour 

marker decline in poor prognosis germ-cell tumours (GETUG 13): a phase 3, multicentre, randomised trial. 


Background: Poor prognosis germ-cell tumours are only cured in about half of patients. We aimed to assess whether treatment intensification based on an early tumour marker decline will improve progression-free survival for patients with germ-cell tumours.

Methods: In this phase 3, multicentre, randomised trial, patients were enrolled from France (20 centres), USA (one centre), and Slovakia (one centre). Patients were eligible if they were older than 16 years, had evidence of testicular, retroperitoneal, or mediastinal non-seminomatous germ cell tumours based on histological findings or clinical evidence and highly elevated serum human chorionic gonadotropin or alpha-fetoprotein concentrations that matched International Germ Cell Cancer Consensus Group poor prognosis criteria. After one cycle of BEP [intravenous cisplatin [20 mg/m(2) per day for 5 days], etoposide [100 mg/m(2) per day for 5 days], and intramuscular or intravenous bleomycin [30 mg per day on days 1, 8, and 15], patients’ human chorionic gonadotropin and alpha-fetoprotein concentrations were measured at day 18-21. Patients with a favourable decline in human chorionic gonadotropin and alpha-fetoprotein continued BEP (Fav-BEP group) for 3 additional cycles, whereas patients with an unfavourable decline were randomly assigned (1:1) to receive either BEP (Unfav-BEP group) or a dose-dense regimen (Unfav-dose-dense group), consisting of intravenous paclitaxel (175 mg/m(2) over 3 h on day 1) before BEP plus intravenous oxaliplatin (130 mg/m(2) over 3 h on day 10; two cycles), followed by intravenous cisplatin (100 mg/m(2) over 2 h on day 1), intravenous ifosfamide (2 g/m(2) over 3 h on days 10, 12, and 14), plus mesna (500 mg/m(2) at 0, 3, 7 and 11 h), and bleomycin (25 units per day, by continuous infusion for 5 days on days 10-14), with granulocyte-colony stimulating factor (lenograstim) support. Centrally blocked computer-generated randomisation stratified by centre was used. The primary endpoint was progression-free survival and the efficacy analysis was done in the intention-to-treat population. The planned trial accrual was completed in May, 2012, and follow-up is ongoing. This study is registered with ClinicalTrials.gov, number NCT01049676.

Findings: Between Nov 28, 2003, and May 16, 2012, 263 patients were enrolled and 254 were available for tumour marker assessment. Of these 51 (20%) had a favourable marker assessment, and 203 (80%) had an unfavourable tumour marker decline; 105 were randomly assigned to the Unfav-dose-dense group and 98 to the Unfav-BEP group. 3-year progression-free survival was 59% (95% CI 49-68) in the Unfav-dose-dense group versus 48% (38-59) in the Unfav-BEP group (HR 0.66, 95% CI 0.44-1.00, P=0.05). 3-year progression-free survival was 70% (95% CI 57-81) in the Fav-BEP group (HR 0.66, 95% CI 0.49-0.88, P=0.01) for progression-free survival compared with the Unfav-BEP group. More grade 3-4 neurotoxic events (seven [7%] vs one [1%]) and haematotoxic events occurred in the Unfav-dose-dense group compared with the Unfav-BEP group. The most common drug-related adverse events were hand-foot skin reaction (20%), diarrhoea (17%), and rash (8%).

Conclusion: Sunitinib was generally well tolerated and provided clinical benefit in a large, diverse population of patients with advanced RCC treated in routine clinical practice.


Personalizing, not patronizing: the case for patient autonomy by unbiased presentation of management options in stage I testicular cancer. 


Testicular cancer (TC) is the most common neoplasm in males aged 15-40 years. The majority of patients have no evidence of metastases at diagnosis and thus have clinical stage I (CS-I) disease
[Oldenburg J, Fossa SD, Nuver J et al. Testicular seminoma and non-seminoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013; 24(Suppl 6): vi125-vi132; de Wit R, Fizazi K. Controversies in the management of clinical stage I testis cancer. J Clin Oncol 2006; 24: 5482-5492]. Management of CSI TC is controversial and options include surveillance and active treatment. Different forms of adjuvant therapy exist, including either one or two cycles of carboplatin chemotherapy or radiotherapy for seminoma and either one or two cycles of cisplatin-based chemotherapy or retroperitoneal lymph node dissection for non-seminoma. Long-term disease-specific survival is 99% with any of these approaches, including surveillance. Weighting the net benefits of surveillance against those of adjuvant treatment depends on prioritizing competing aims such as avoiding unnecessary treatment, avoiding more burdensome treatment with salvage chemotherapy and minimizing the anxiety, stress and life disruption associated with relapse. Unbiased information about the advantages and disadvantages of surveillance and adjuvant treatment is a prerequisite for informed consent by the patient. In a clinical scenario like CSI TC, where different disease-management options produce indistinguishable long-term survival rates, patient values, priorities and preferences should be taken into account.

In this review, we provide an overview about risk factors for relapse, potential benefits and harms of adjuvant chemotherapy and active surveillance and a rationale for involving patients in individualized decision making about their treatment rather than adopting a uniform recommendation for all.


KARCINÓM PRSNÍKA

KARCINÓM PĽÚC

Masarykova A, Scepanovic D, Povinec P, Bires P, Pobijakova M.
Use of 18 FDG PET/CT in the radiotherapy planning of lung cancer – our updated experiences. XIV Central European Lung Cancer Conference, 29.11. - 02.12.2014, Vienna, Austria (poster)