

- *September 1976*

First Meeting

EORTC Soft Tissue Sarcoma Cooperative Group

- *October 1976*

First patient recruited to study 62761

- *September 1978*

merged with

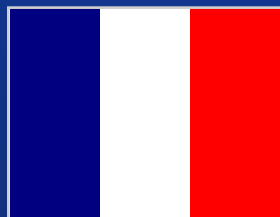
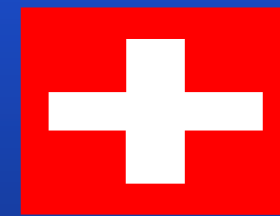
International Osteosarcoma Group

EORTC Soft Tissue and Bone Sarcoma Group

Founding members (1976)



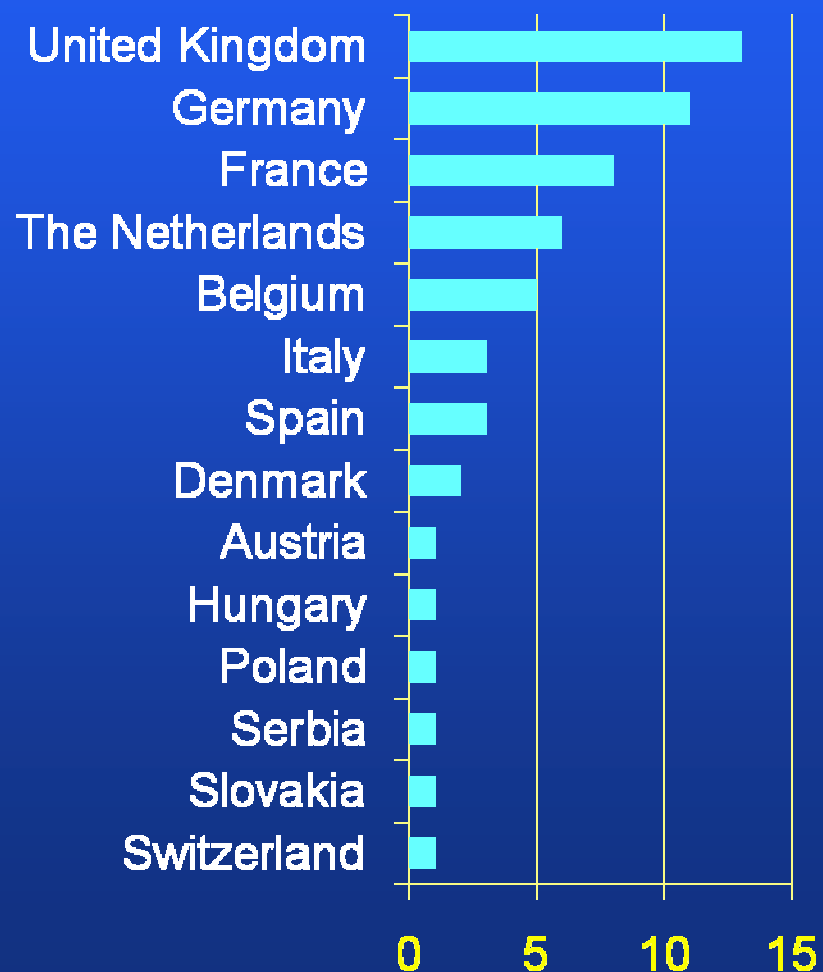
G. Bonadonna, G. Booy, D. Crowther,
E. Engelsman, C. Jasmin, Y. Kenis,
J. Mulder, A. T. van Oosterom, H. M.
Pinedo, L. M. van Putten, P. J.
Schmidt, S. Seeber, J. H. Senn,
R. Sylvester, J. A. M. van Unnik,
C. Vendrik, Th. Wagener,
W. Wilmanns



STBSG in the year 2010

- **57 institutions**
- **14 countries**
- **multidisciplinary**
 - medical oncologists
 - radiation oncologists
 - surgical/orthopedic oncologists
 - pathologists
 - radiologists
- **full membership:**
 - 5 new patients/year

Countries involved

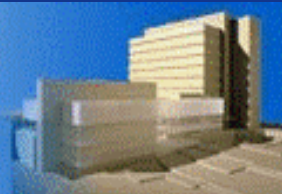




Centre
d'Investigation
Clinique en
Cancérologie



NCIC Clinical Trials Group
NCIC Groupe des essais cliniques



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EORTC Soft Tissue and Bone Sarcoma Group

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- **Systemic Treatment**
Chair: Peter Reichardt, Berlin
- **Local Treatment**
Chair: Alessandro Gronchi, Milano
- **Pathology and TL-Research**
Chair: A.P. deiTos, Treviso
- **Functional Imaging**
Chair: Winette van der Graaf, Nijmegen
- **Bone Tumors**
Sophie Piperno-Neumann, Paris
Hans Gelderblom, Leiden

- **Phase II studies in osteosarcoma**
methotrexate, cisplatin, ifosfamide (62832), iproplatin (62862)
- **80931 - Phase III randomized trial of chemotherapy with or without GCSF in operable osteosarcoma** EORTC/MRC/SIOP/UKCCSG/CSG
- **EOI Osteosarcoma phase II**
Aug 93 – Sep 02 (mit MRC, UKCCSG, CSG, SIOP)
- **62981 Euro-EWING phase III**
with GPOH, UKCCSG, SFOP, SIAK
- **62993 Phase II study to evaluate the role of weekly cisplatin with oral Etoposide in Ewing's sarcoma and primitive neuroectodermal tumour (PNET)** with metastasis outside the lung and the pleura
- **62911 Phase II study of liposomal muramyl tripeptide phosphatidyl-ethanolamine (MTP/PE) in advanced soft tissue sarcoma of the adult**

A phase II multicenter study evaluating efficacy of pazopanib in advanced bone sarcomas (BS)

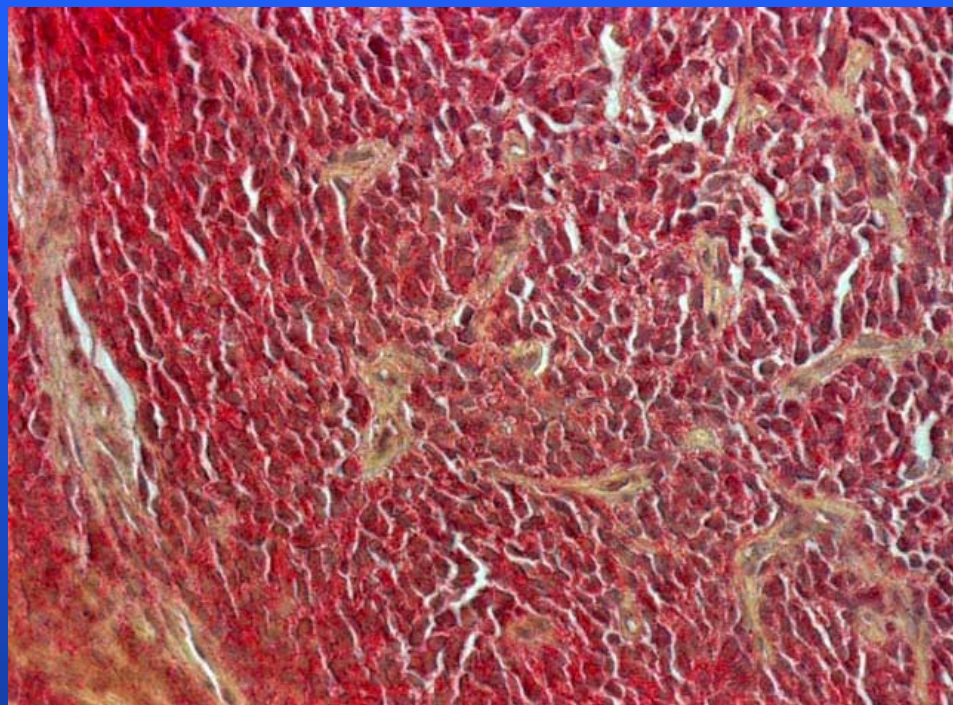
SC: Piotr Rutkowski

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Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland (550)

A phase II multicenter study evaluating efficacy of pazopanib in advanced bone sarcomas (BS)



(b) Section from an Ewing's sarcoma specimen with high VEGF-A expression. Original magnification 400x.

Kreuter et al. Eur J Cancer 2006 ↑
Kreuter et al. Clin Cancer Res 2006 →

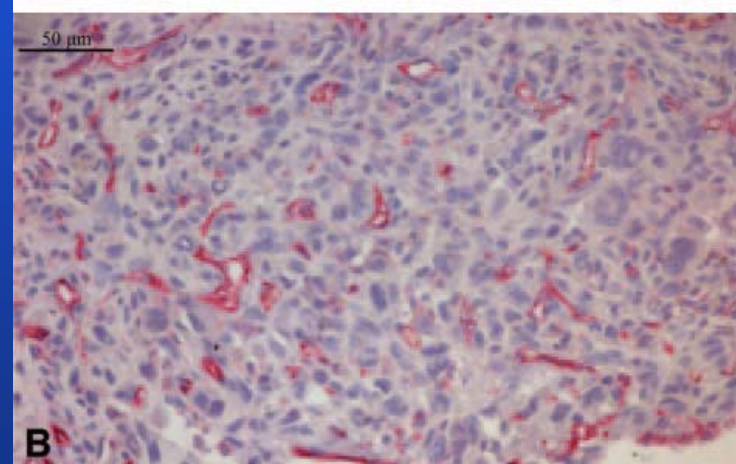
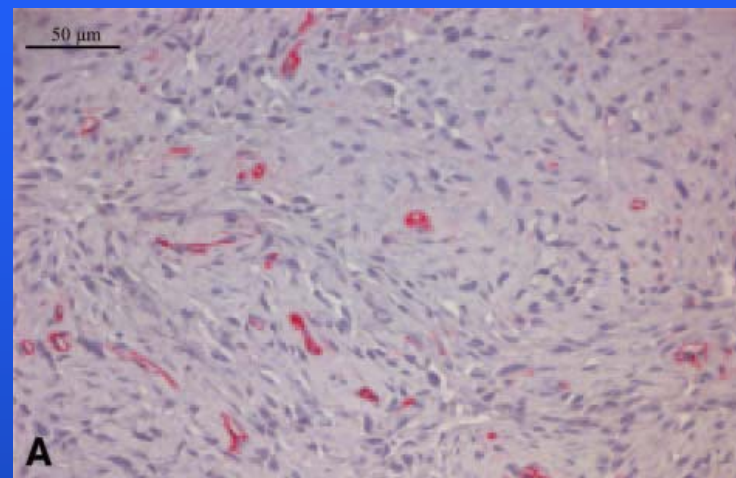


Fig. 2 Immunohistochemical staining of osteosarcoma tissue slides with anti-CD31 antibodies for quantification of MVD. A, section from an osteosarcoma specimen with low intratumoral MVD. B, section from an osteosarcoma specimen with high intratumoral MVD. Original magnification, ×200.

Rationale:

- No standard of care (EU/US) for relapsing BS
- Strong biological rationale supporting the key role of Angiogenesis in BS progression
 - ◆ DuBois et al. Cancer 2007; 109: 813-9
 - ◆ Kreuter et al. Clin Cancer Res 2004; 10: 8531-8537
 - ◆ Rutkowski et al. J Surg Oncol 2003; 84: 151-159
 - ◆ Kaya et al. Clin Cancer Res 2000; 6:572-577
 - ◆ Kalinski et al. Cancer 2006; 106: 2028-2038
 - ◆ Reddy et al. Angiogenesis 2008; 11: 257-267
- Diffusion of pazopanib in bone/cartilagineous tissues

Rationale:

- Pazopanib (GW786034) = inhibitor of receptor tyrosine kinases (mainly VEGFR-1,-2,-3...)
 - Phase III : RCC, ovarian cancer, NSCLC, advanced breast cancer, soft tissue sarcomas....
 - Promising agent for advanced/metastatic soft tissue sarcoma (Sleijfer et al. J Clin Oncol 2009; 27: 3126-3132)
-
- Drug: Pazopanib 800 mg per day until confirmed disease progression, unacceptable toxicity or patient refusal

4 Strata:

Osteosarcoma, Chondrosarcoma, Ewing Sarcoma, High-Grade Spindle cells BS

Primary objective

Efficacy/Safety of Pazopanib → PFS @ 12 weeks and 24 weeks (RECIST 1.1)

Secondary objectives

- Objective response rate (CR, PR) and non-progression rate (CR+PR+SD)
- Duration of response
- Safety profile (CTC-AE, version 3.0)
- Overall survival

Exploratory translational research

- Correlation response/Biomarkers (angiogenesis/cytokines) same as EORTC 62043/62072 (pazopanib in soft tissue sarcomas)
- To investigate the intratumoral microvessel density on pretherapeutic FFPE material
- **Correlative imaging study**

Main eligibility criteria

- **Metastatic high-grade BS (based on local pathologist); High grade chondroS (localized, unresectable cases of chondroS can be included), not curable by radiotherapy or surgery**
- **Prior treatment:**
 - for Metastatic Ewing's S, osteoS and other high-grade spindle cell S of bone: at least one line, but no more than 2 prior combination chemotherapy regimens for metastatic disease.
 - for advanced/metastatic chondroS: no prior chemotherapy.
- **Neo-adjuvant/maintenance therapy are not counted towards this requirement**

Main eligibility criteria - 2

- Disease progression (RECIST 1.1) on previous therapy within the last 6 months must be confirmed.
- Measurable disease (RECIST 1.1).
- **Age \geq 18 y.o. [under discussion for young patients]**
- PS 0-1 (or 2 if pain limits mobility)
- Informed consent signed

What are the appropriate statistical assumptions ?

Primary objective

Efficacy/Safety of Pazopanib → PFS @ 12/24 weeks (RECIST 1.1)

	P0	P1
Ewing Sarcoma	?	?
Osteosarcoma	?	?
Chondrosarcoma	??	??
Spindle cells Sarcoma	??	??

