PEDIATRIC SARCOMAS: WHAT'S NEW IN 2015-2016 ?

B. Brichard - N. Corradini
les comités GROUPOS et TMM
de la SFCE

PRESENTATION PLAN

- Adolescents and young adults in studies
- Bone sarcomas
- Soft tissues sarcomas
  - RMS : latest results
  - Non-RMS tumours : update
  - Infantile fibrosarcoma : papers

Adolescents and young adults in studies

Adolescents and young adults

EUROCARE-5-Study

Registry for updating population-based cancer survival in Europe

➢ Sarcoma age-related differences in survival

Trama A, Botta L, Foschi R, Ferrari A, Stiller C, Desandes E, Maule MM, Merletti F, Gatta G. **Survival of European adolescents and young adults diagnosed with cancer in 2000-2007: latest population-based data from EUROCARE-5**. Lancet Oncol, 2016 May 26. pii:S1470-2015(16)00162-5.

- Bisogno G et al. **Rhabdomyosarcoma in adolescents: a report from the AIEOP Soft Tissue Sarcoma Committee**. Cancer 118(3):821-7, 2012
- Joshi D et al. **Age is an independent prognostic factor in rhabdomyosarcoma: a report from the Soft Tissue Sarcoma Committee of the Children's Oncology Group**. Pediatr Blood Cancer. 2004;42:64-73
- Ferrari A et al. **Rhabdomyosarcoma in adults. A retrospective analysis of 171 patients treated at a single institution**. Cancer 98:571-580, 2003
- Sultan I et al. **Comparing adult and pediatric rhabdomyosarcoma in the surveillance, epidemiology and end results program, 1973 to 2005: an analysis of 2,600 patients**. J Clin Oncol 2009, 27(20), 3391-3397
- Ferrari A et al. **Soft tissue sarcoma across the age spectrum: A population-based study from the surveillance epidemiology and end results database**. Pediatric Blood & Cancer, 57(6), 943–949.
- Sultan I, et al. **Comparing children and adults with synovial sarcoma in the Surveillance, Epidemiology and End Results Program, 1983 to 2005: an analysis of 1268 patients**. Cancer 2009;115:3537-3547

Adolescents and young adults

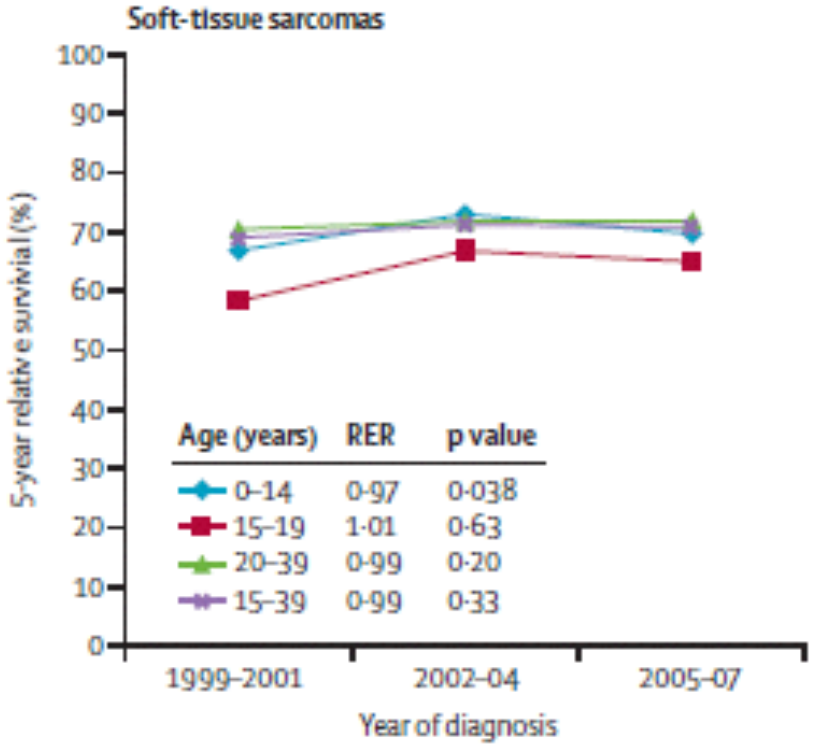
EUROCARE-5-Study (2000-2007)

5-year OS :

RMS : 66.6% (0-14y)
vs 39.6% (15-19y)

Ewing's Sarcoma :
66.6% (0-14y)
vs 51.1% (15-19y)

Osteosarcoma :
66.8% (0-14y)
vs 60.3% (15-19y)



Trama A, et al., Lancet Oncol, 2016 May 26. pii:S1470-2015(16)00162-5.

➔ **Survival of AYA improved over time but…**

➔ Poorer survival in AYA sarcomas justifies initiatives as integrated pediatric-adult multidisciplinary setting

➔ Adolescents and young adults RMS are to be treated in HR groups

Bone sarcomas

EURAMOS -1

A randomized trial of the European and American Osteosarcoma Study Group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy

EURAMOS-1

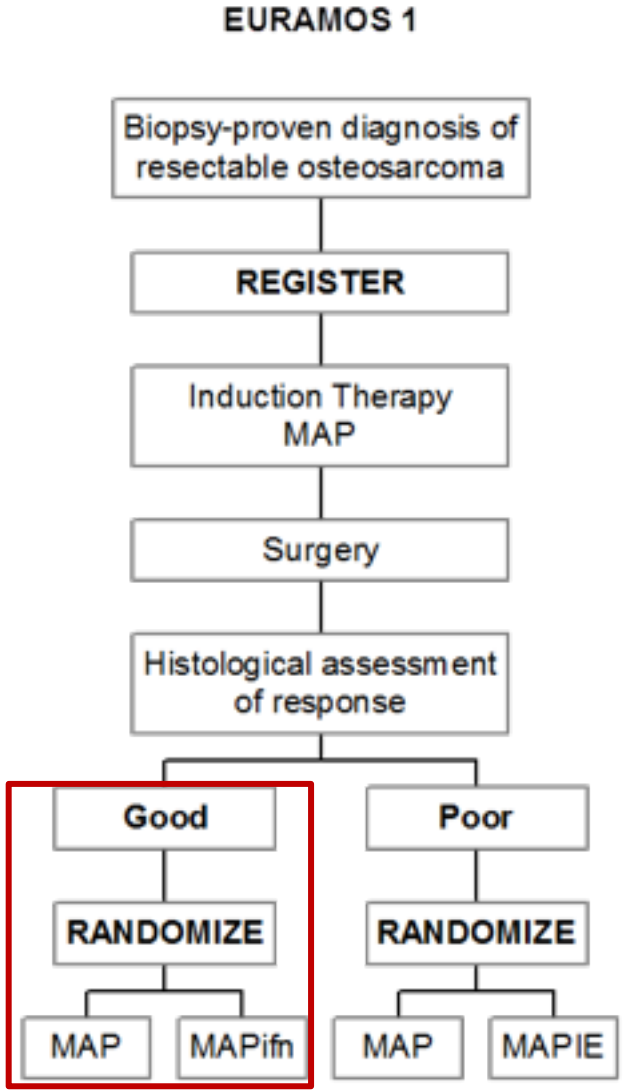
A randomized trial of the European and American Osteosarcoma Study Group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy

Primary Objectives

- Compare MAP vs MAPifn regimen for EFS
  (patients with **good histological response** after pre-operative chemotherapy)
- Compare MAP vs MAPIE regimen for EFS
  (patients with **poor histological response** after pre-operative chemotherapy)

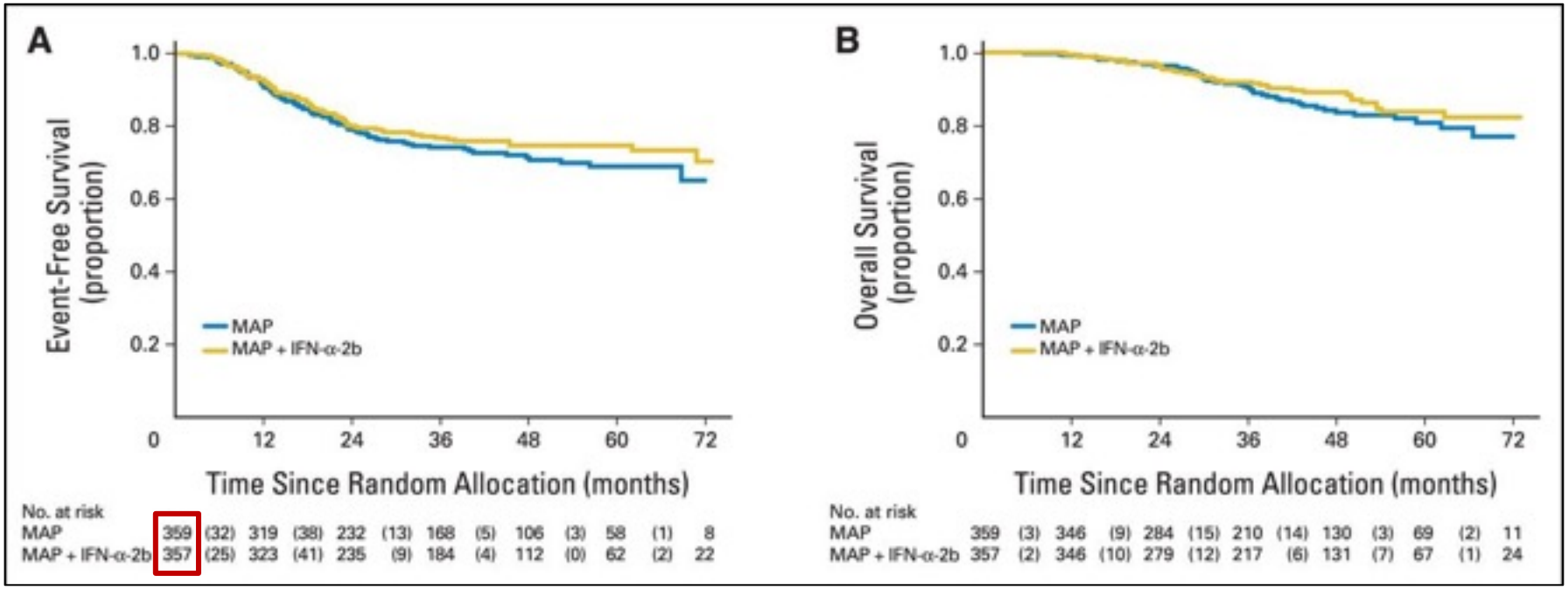
Secondary Objectives

- Investigate whether addition of IE/ifn-α-2b in maintenance chemotherapy improves :
  - OS
  - Toxicity (short and long-term)
  - QoL



EURAMOS-1

Analysis of patients with good response to preoperative chemotherapy



Bielack S. et al., J Clin Oncol. 2015 Jul 10;33(20):2279-87.

Addition of ifn-α-2b to postoperative chemotherapy didn't improve EFS nor OS
(Long-term FU for events and survival continues)

EURAMOS-1

A randomized trial of the European and American Osteosarcoma Study Group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy

Primary Objectives

- Compare MAP vs MAPifn regimen for EFS
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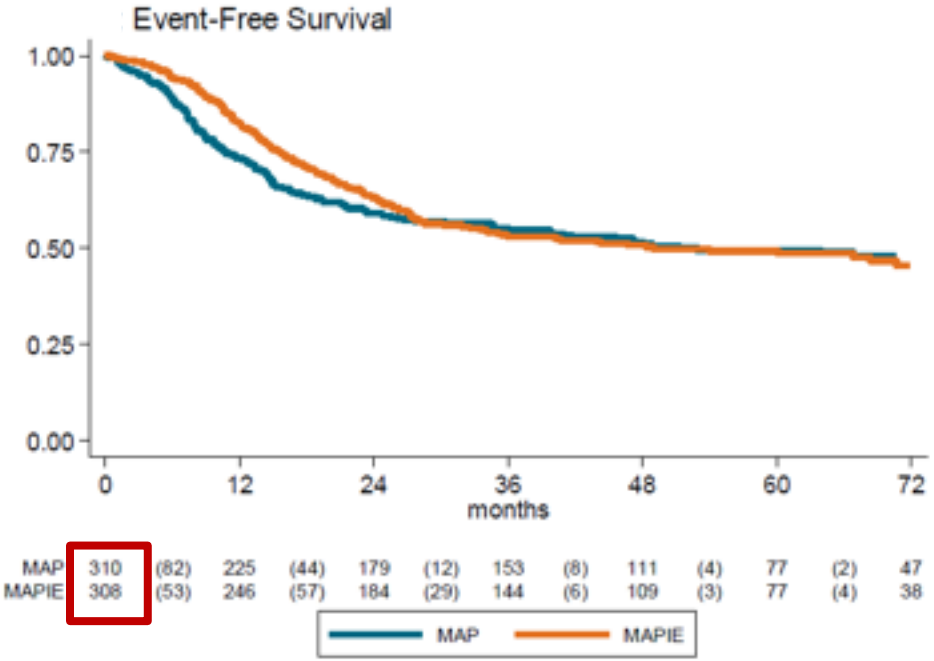
  (patients with **poor histological response** after pre-operative chemotherapy)

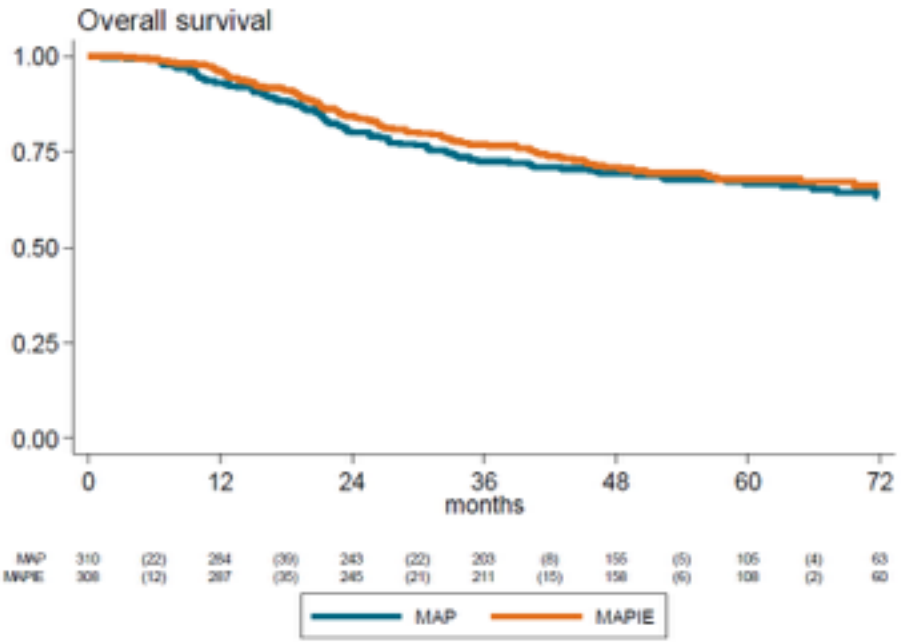
Secondary Objectives

- Investigate whether addition of IE/ifn-α-2b in maintenance chemotherapy improves :
  - OS
  - Toxicity (short and long-term)
  - QoL

EURAMOS-1

Analysis of patients with poor response to preoperative chemotherapy





Addition of IE to postoperative chemotherapy didn't improve EFS nor OS and is associated with increased toxicity

Randomised Phase III Comparison of MAPIE vs MAP in patients with a Poor Response to pre-operative chemotherapy for newly-diagnosed high-grade osteosarcoma: results from the EURAMOS-1 Trial
MANUSCRIPT in press (Lancet Oncol)

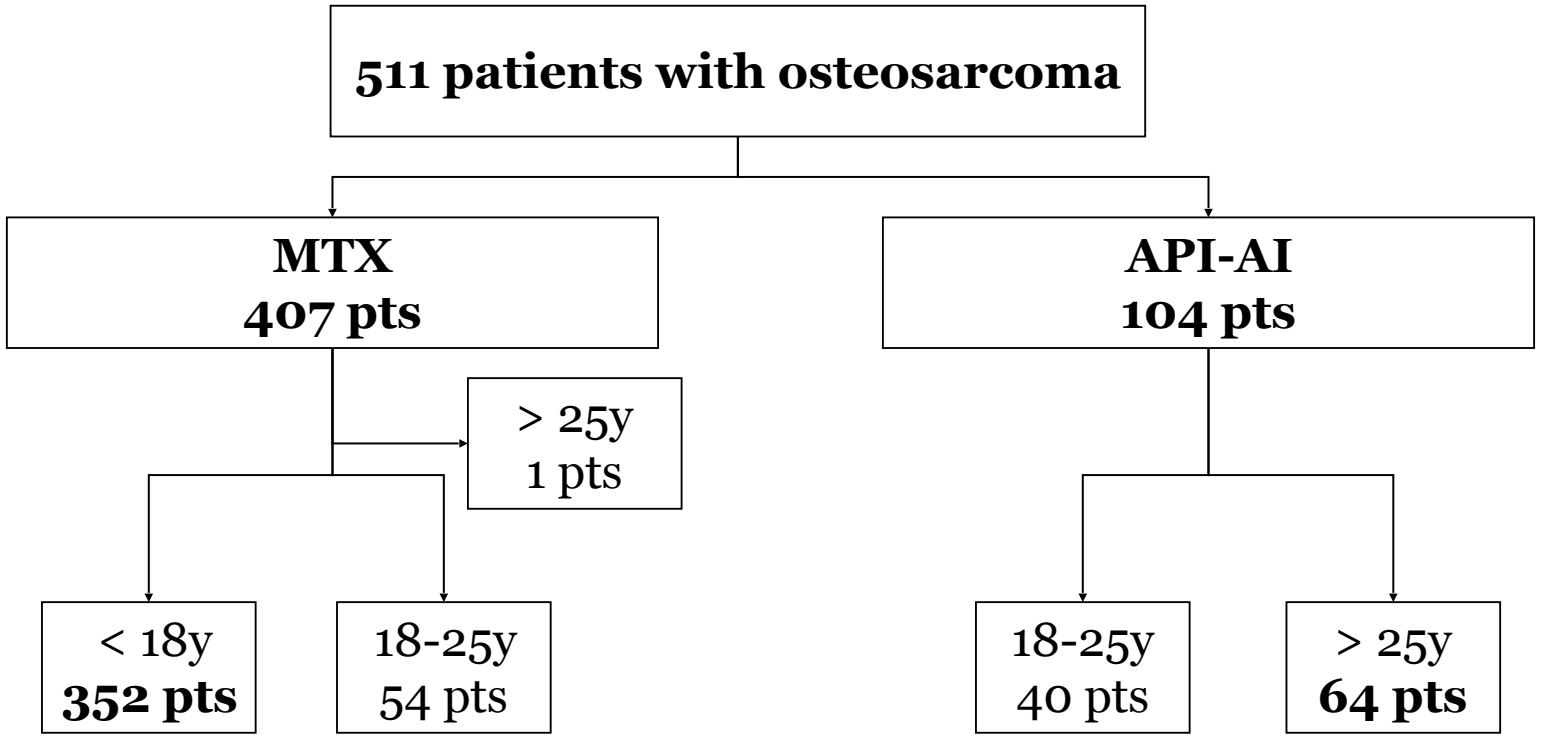
OS2006

MTX-based and API-AI protocols

Preliminary results
February 2016

OS2006

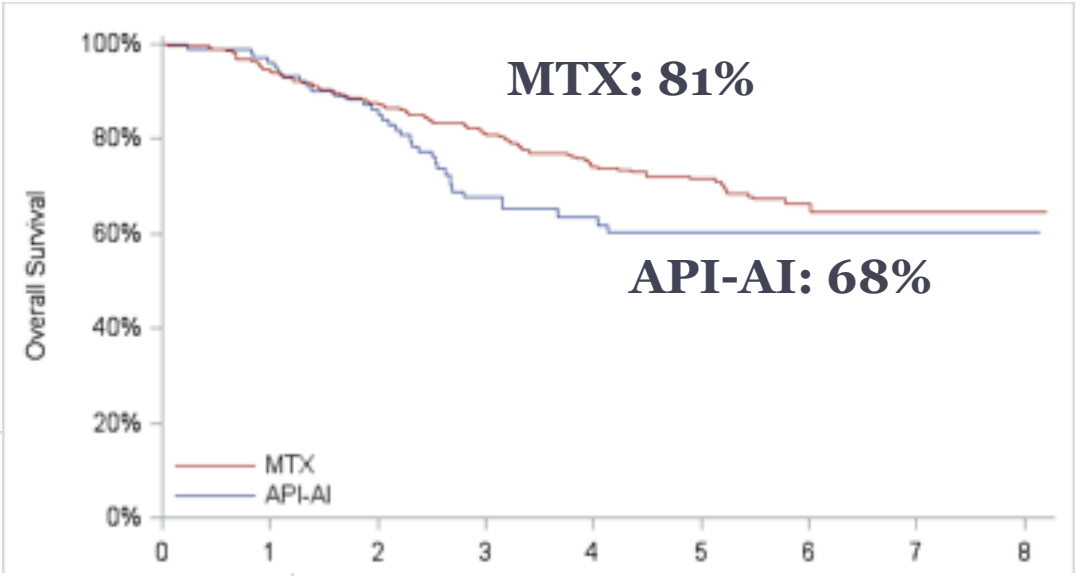
MTX-based and API-AI protocols



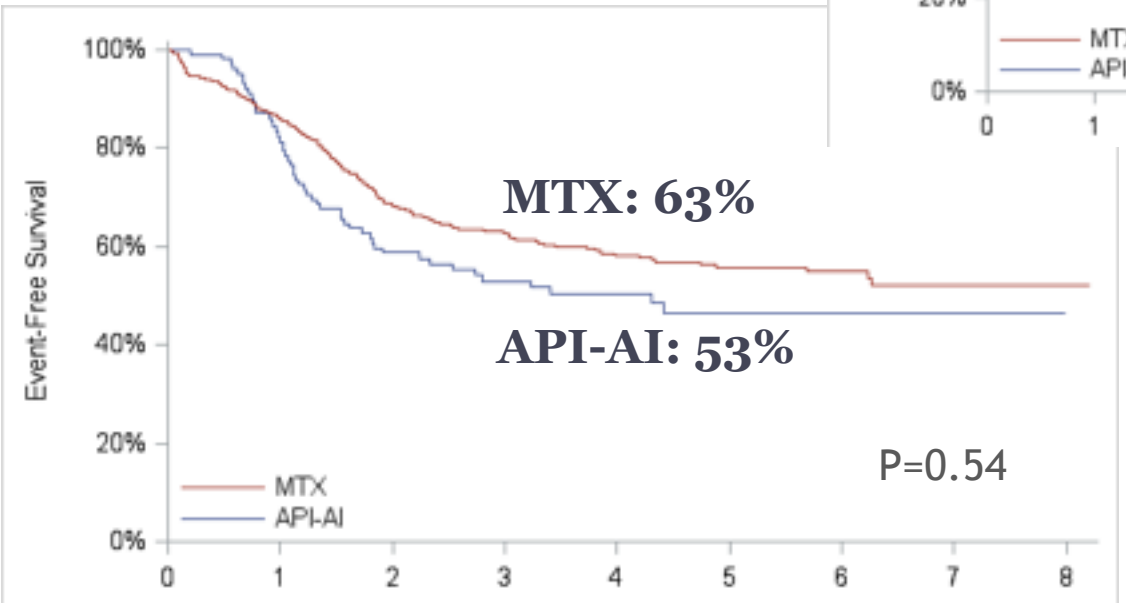
OS2006

MTX-based and API-AI protocols

Overall Survival



EFS (18-25y)

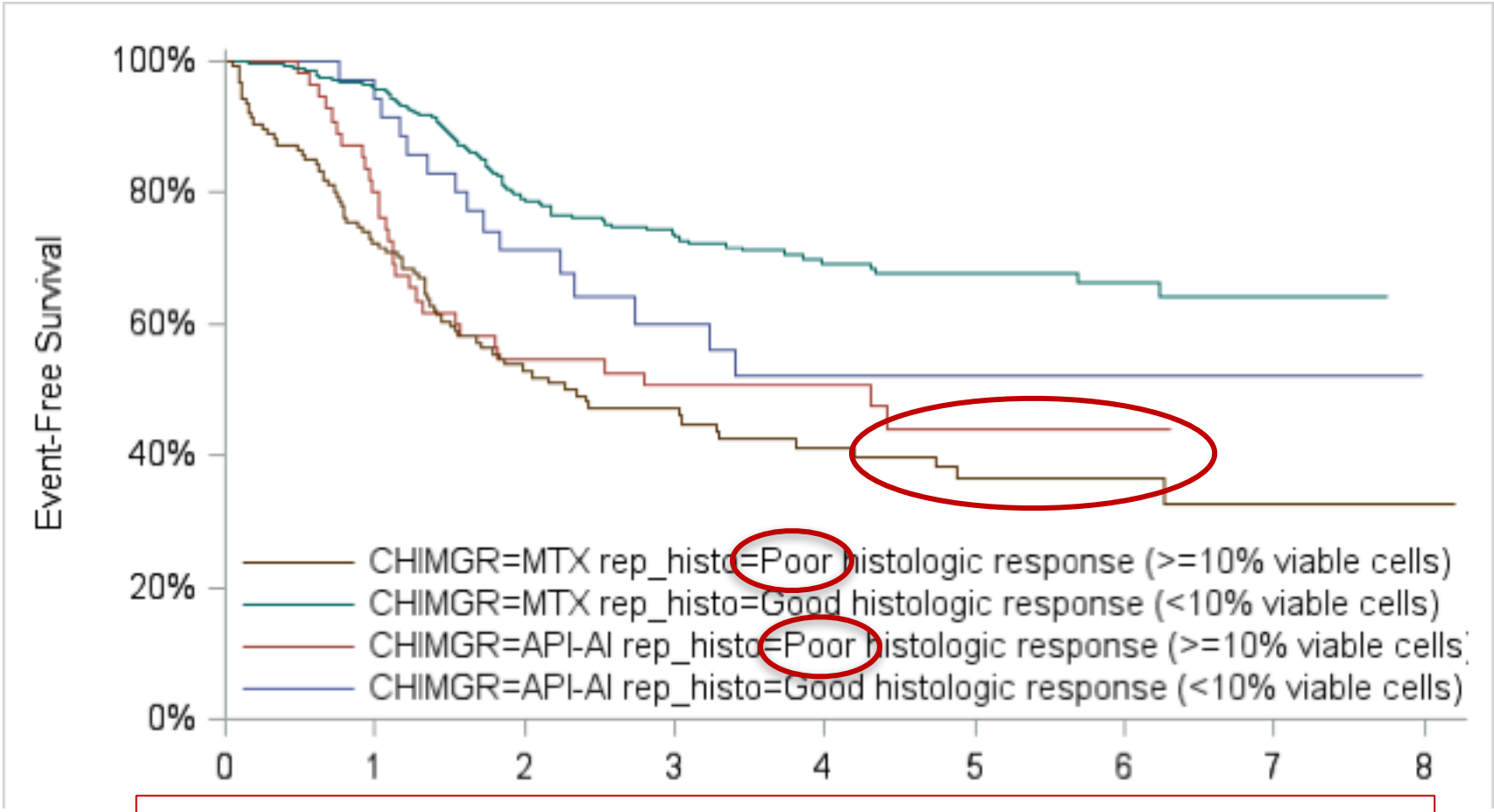


➔ No significant difference between the two treatments regardless of the group and age stratification

OS2006

MTX-based and API-AI protocols

EFS by **chemotherapy** group and **histologic** response



➔ EFS lower in patients with poor histologic response in both treatment groups

OS2006

MTX-based protocol

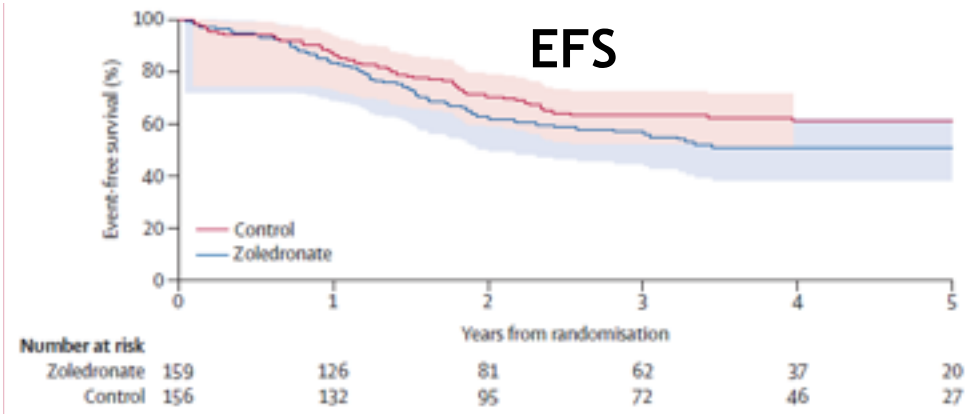
OS by **localised/metastases** group and **histologic** response

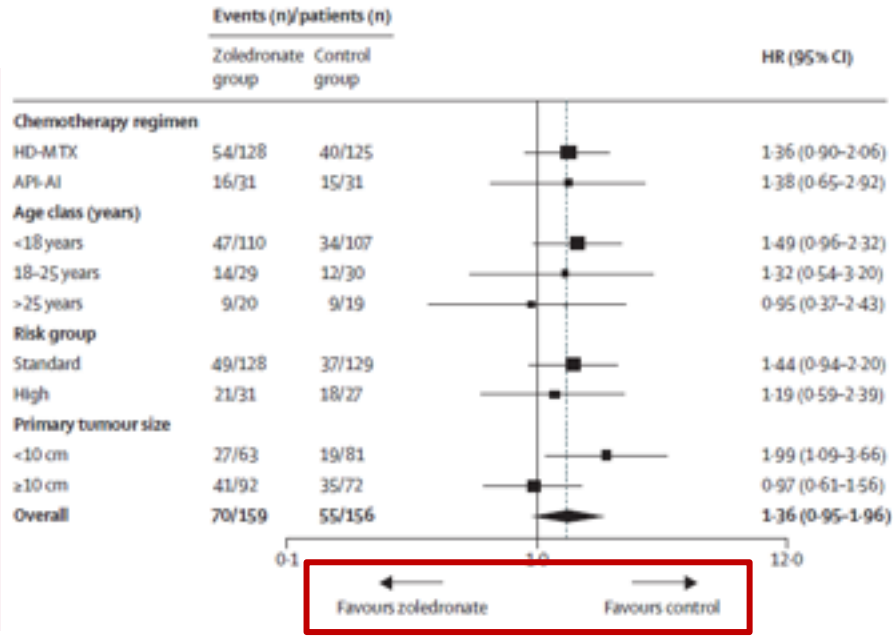
➔ OS lower in patients with poor histologic response and metastases

OS2006: Preview results

Zoledronate in combination with chemotherapy and surgery to treat osteosarcoma (OS2006): a randomised, multicentre, open-label, phase 3 trial

Sophie Piperno-Neumann, Marie-Cécile Le Deley, Françoise Rédini, Hélène Pacquement, Perrine Marec-Bérard, Philippe Petit, Hervé Brisse, Cyril Lervat, Jean-Claude Gentet, Natacha Entz-Werlé, Antoine Italiano, Nadège Corradini, Emmanuelle Bompas, Nicolas Penel, Marie-Dominique Tabone, Anne Gomez-Brouchet, Jean-Marc Guinebretière, Eric Mascard, François Gouin, Aurélie Chevance, Naïma Bonnet, Jean-Yves Blay, Laurence Brugières, on behalf of the Sarcoma Group of UNICANCER, the French Society of Pediatric Oncology (SFCE), and the French Sarcoma Group (GSF-GETO)

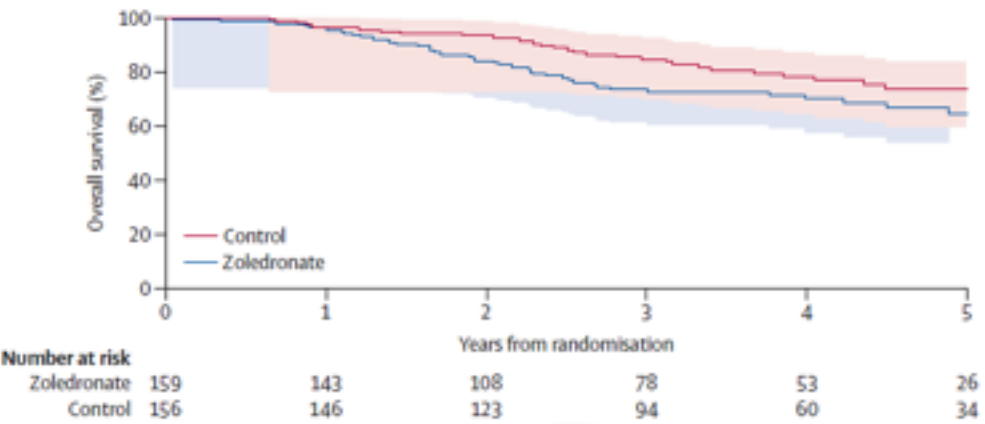




3-year event-free survival was 63.4% (55.2-70.9)
for the control group and 57.1% (48.8-65.0) for the zoledronate group.
The risk of failure was not reduced and was even marginally higher in the zoledronate group than in the control group (hazard ratio [HR] 1.36 [95% CI 0.95-1.96]; p=0.094).

OS2006: Preview results

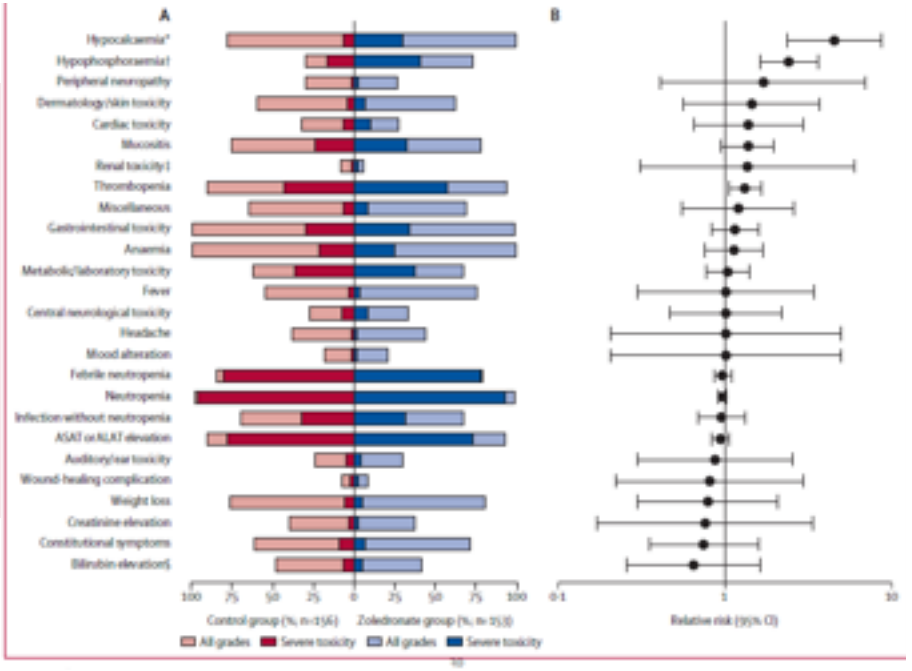
Overall Survival



3-year overall survival was 84.4% (77.3-89.6) in the control group and 73.4% (65.2-80.2) in the zoledronate group (1.61 [0.995-2.61]; p=0.052).

L. Brugières, S Piperno-Neumann

Toxicities



No significant increase in acute toxicity in the zoledronate group, except:

- **a large excess of hypocalcaemia and hypophosphoremia (p<0.0001)**
- **a slight increase of thrombocytopenia.**

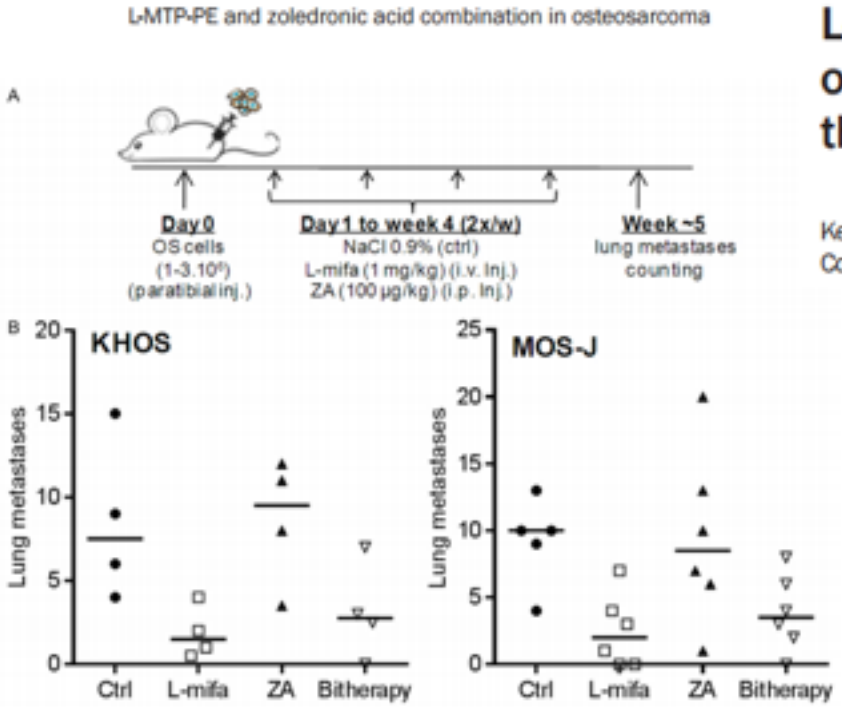
Osteosarcoma : biology

Am J Cancer Res 2016;6(3):677-689
www.ajcr.us /ISSN:2156-6976/ajcr0025208

Original Article

L-MTP-PE and zoledronic acid combination in osteosarcoma: preclinical evidence of positive therapeutic combination for clinical transfer

Kevin Biteau[1,2], Romain Guiho[1,2], Mathias Chatelais[1,2], Julien Taurelle[1,2], Julie Chesneau[1,2], Nadège Corradini[1,2,3], Dominique Heymann[1,2], Françoise Redini[1,2,4]



- ➔ L-mifamurtide seems to inhibit lung metastasis dissemination in OS mice models.
- ➔ Zometa induces bone protection effect
- ➔ No interference showed between these two drugs
- ➔ Promising therapeutic effect ?

Osteosarcoma : new surgical aspect

Ann Surg Oncol. 2016 Apr;23(4):1380-6. doi: 10.1245/s10434-015-4988-z. Epub 2015 Nov 20.

Percutaneous Computed Tomography-Guided Thermal Ablation of Pulmonary Osteosarcoma Metastases in Children.

Yevich S[1], Gaspar N[2], Tselikas L[3,4], Brugières L[2], Pacquement H[5], Schleiermacher G[5], Tabone MD[6], Pearson E[3], Canale S[7], Muret J[8], de Baere T[3,4], Deschamps F[3,4].

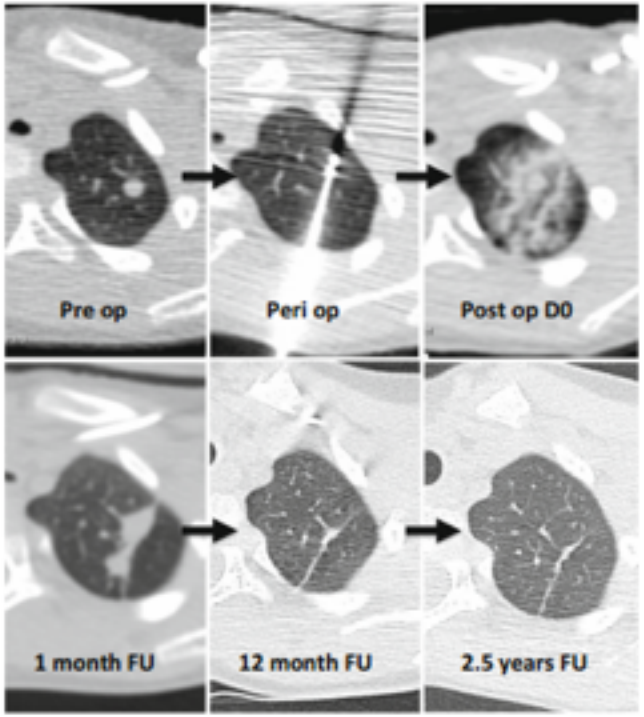
Conclusion : Percutaneous thermal ablation is a safe and effective minimally-invasive **curative** local treatment alternative for children with oligometastatic osteosarcoma in whom surgical intervention is clinically contraindicated or unappealing

Radiofrequency Ablation of Metastases from Osteosarcoma in Patients Under 25 Years: The SCFE Experience

L. Saumet, F. Deschamps, P. Marec-Berard, N. Gaspar, N. Corradini, P. Petit, N. Sirvent & L. Brugières

Pediatr Hematol Oncol. 2015 Feb;32(1):41-9

Conclusion : RFA is feasible in AYA with osteosarcoma. Its role in the curative care of small secondary bone lesions remains to be confirmed.



EURO-E.W.I.N.G. 99

A randomized, prospective, multi-centre, international study, linking several co-operative groups, to improve outcome in patients with Ewing tumour.

ukccsg

GESELLSCHAFT FÜR PÄDIATRISCHE ONKOLOGIE UND HÄMATOLOGIE GPOH

SIAK

SFCE

EORTC
European Organization for Research and Treatment of Cancer

In collaboration with

EBMT

EURO-E.W.I.N.G. 99

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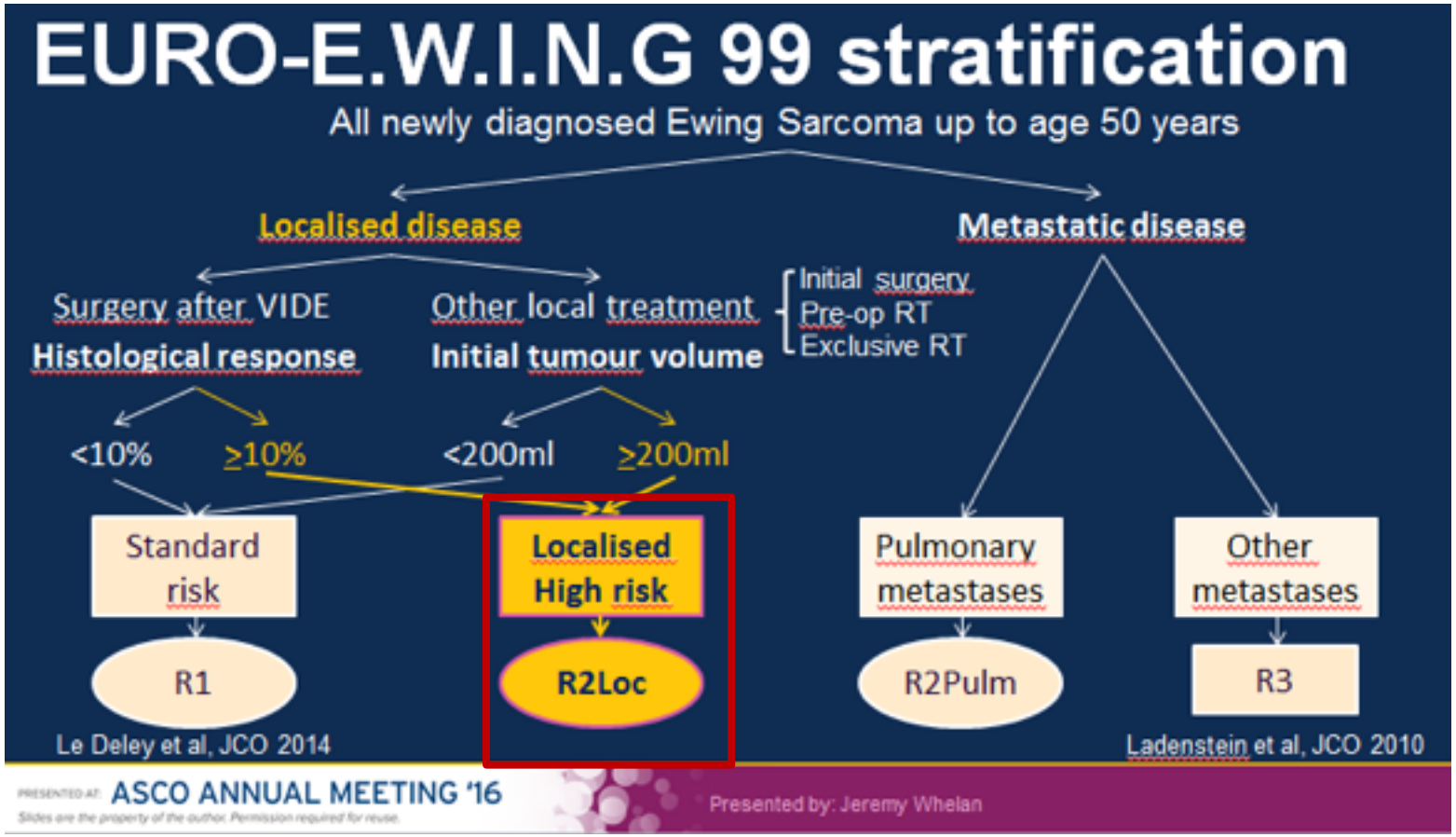
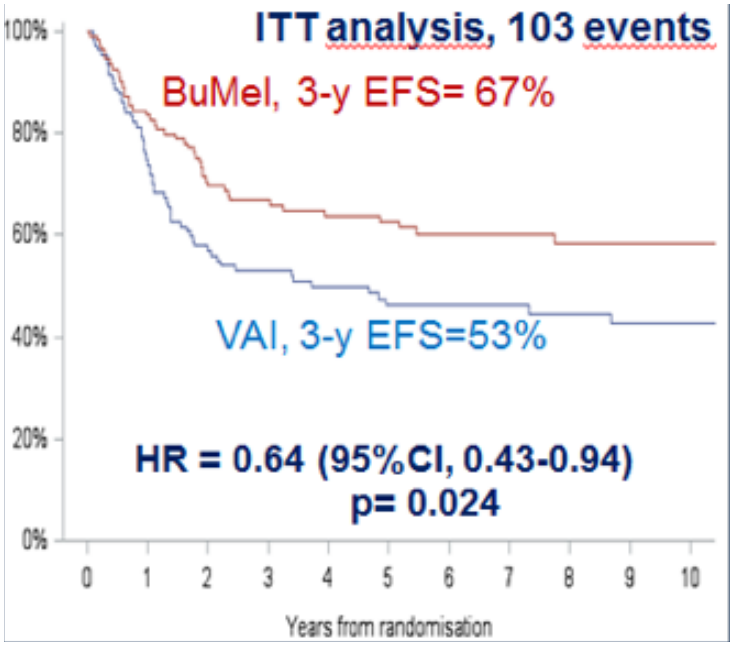
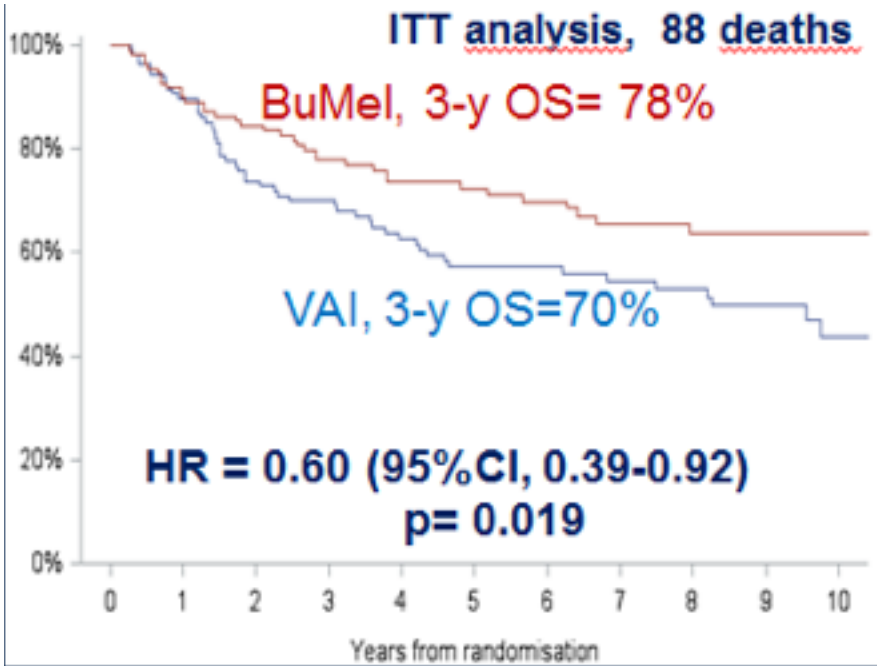


EURO-E.W.I.N.G. 99

EFS



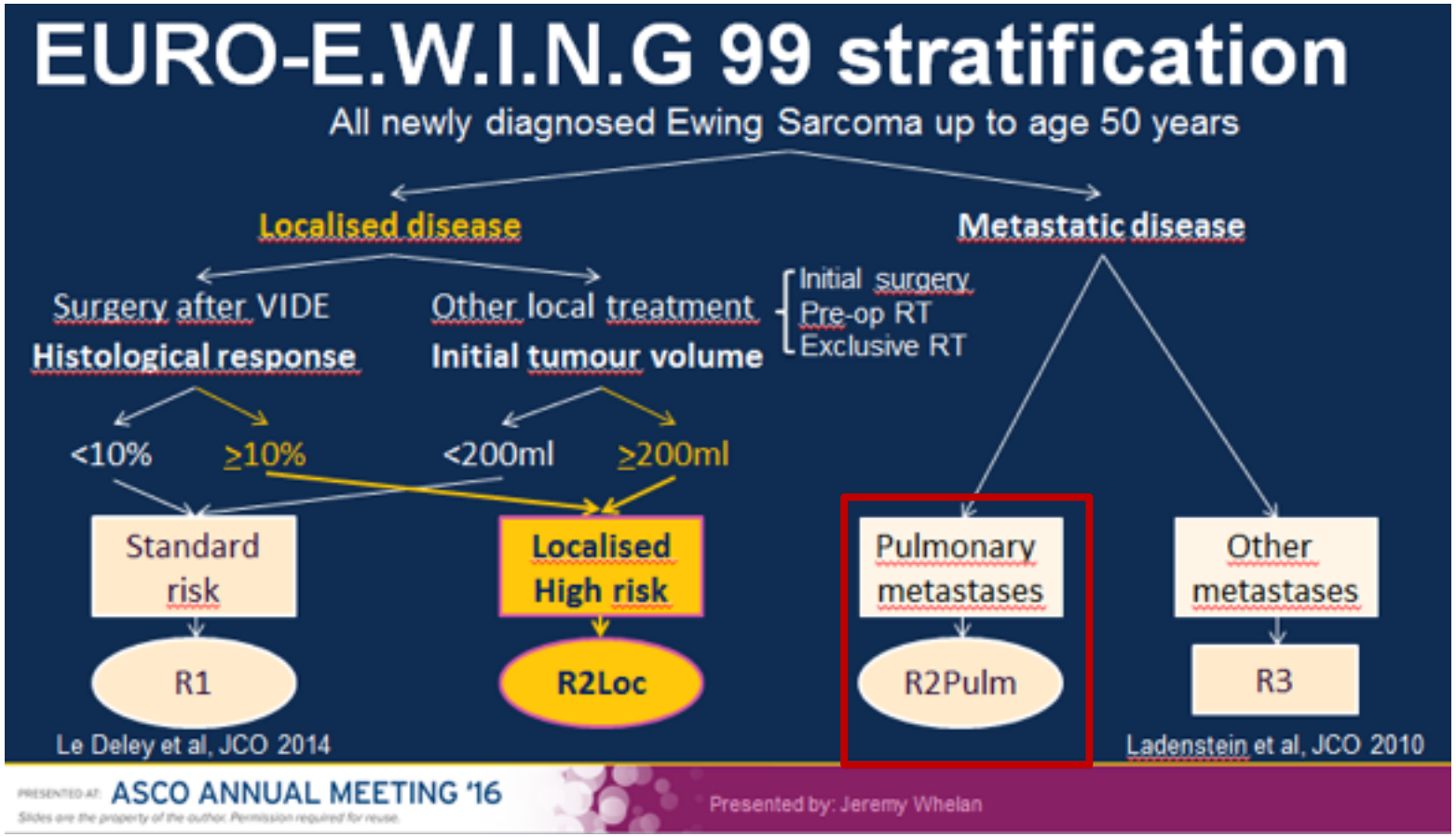
Overall survival



➔ Significant improvement of EFS and OS with BuMel compared to standard chemotherapy alone in R2loc

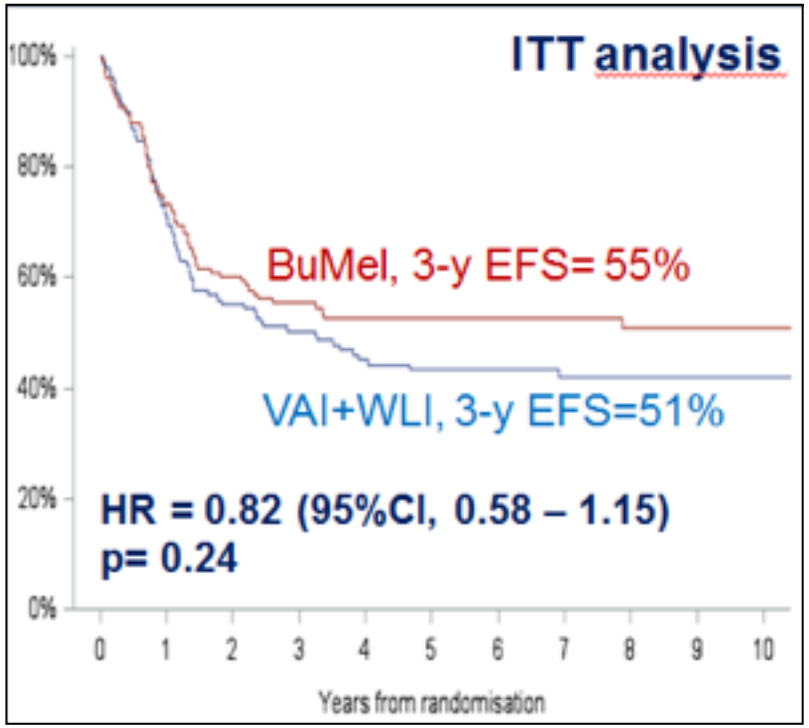
EURO-E.W.I.N.G. 99

A randomized, prospective, multi-centre, international study, linking several co-operative groups, to improve outcome in patients with Ewing tumour.

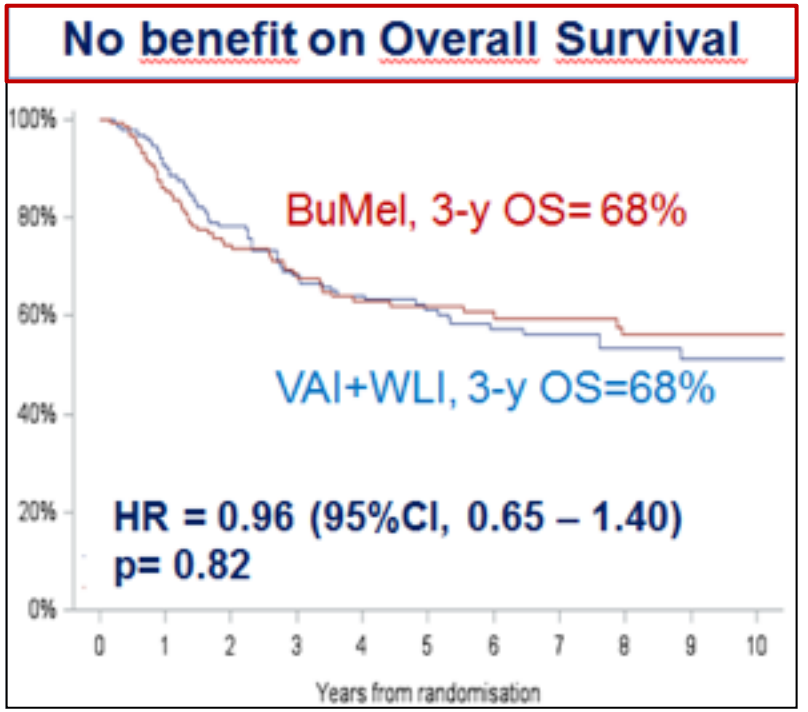


EURO-E.W.I.N.G. 99

EFS



Overall survival



➔ No significant improvement of EFS and OS with BuMel compared to standard chemotherapy + whole lung irradiation in R2pulm

EURO-E.W.I.N.G. 99

CONCLUSIONS

- BuMel therapy showed significant improvement of EFS and OS and therefore should be considered as a standard of care for **R2loc** patients
- BuMel therapy didn't showed any improvement in EFS or OS compared to standard chemotherapy + WLI for **R2pulm** patients
- Data about long term toxicities are not yet available

BUT…

- Several remarks about these results should be kept in mind:
  - Less than 50% of the eligible patients were randomised
  - Final analysis has been performed before full enrolment and end of follow up
  - Conclusions of this trial might be influenced by institutional practices

➔ Therefore, BuMel therapy results need further validation from other groups using different treatment approaches such as dose dense schedule without transplant.

➔ BuMel will be included in EE2012 trial for R2loc patients (ongoing amendment september 2016)

Ewing Sarcoma : review

VOLUME 33 · NUMBER 27 · SEPTEMBER 20 2015

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Ewing Sarcoma: Current Management and Future Approaches Through Collaboration

Nathalie Gaspar, Douglas S. Hawkins, Uta Dirksen, Ian J. Lewis, Stefano Ferrari, Marie-Cecile Le Deley, Heinrich Kovar, Robert Grimer, Jeremy Whelan, Line Claude, Olivier Delattre, Michael Paulussen, Piero Picci, Kirsten Sundby Hall, Hendrik van den Berg, Ruth Ladenstein, Jean Michon, Lars Hjorth, Ian Judson, Roberto Luksch, Mark L. Bernstein, Perrine Marec-Bérard, Bernadette Brennan, Alan W. Craft, Richard B. Womer, Heribert Juergens, and Odile Oberlin

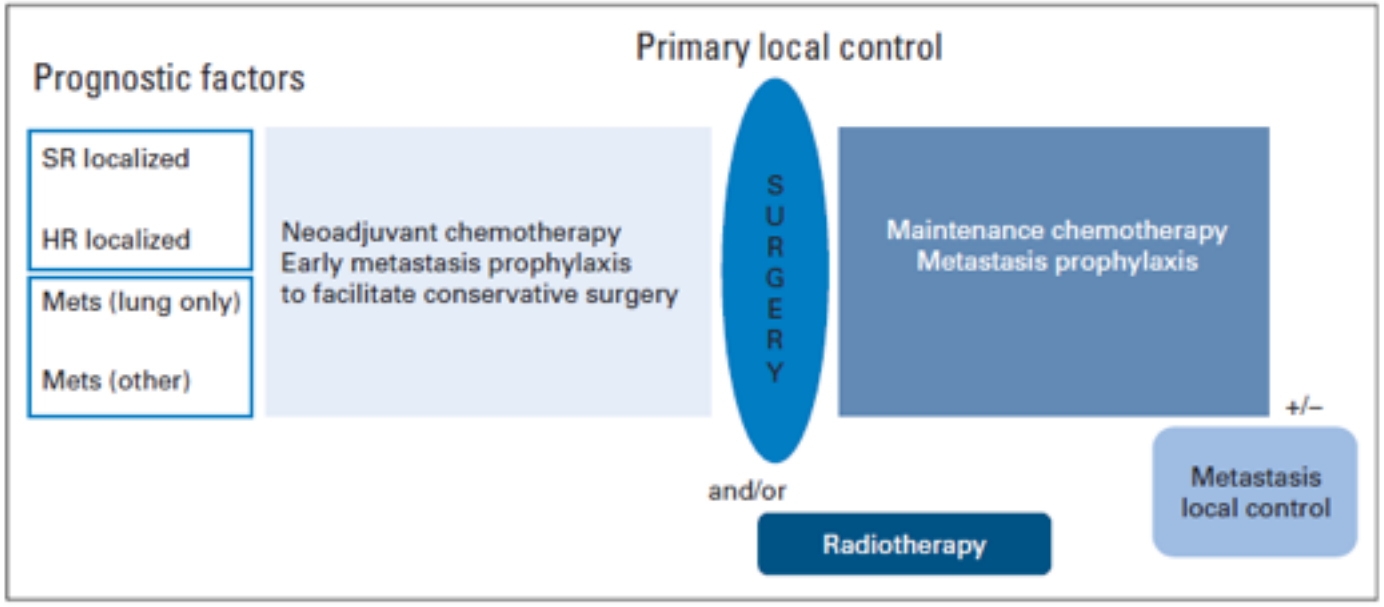


Fig 2. Current risk-adapted treatment strategy in Ewing sarcoma (ES). Strategy is adapted to metastatic status in North America, metastatic status and type of metastasis, and histologic response or initial tumor volume in localized ES in Europe. HR, high risk; Mets, metastasis; SR, standard risk.

Ewing Sarcoma : some new targets

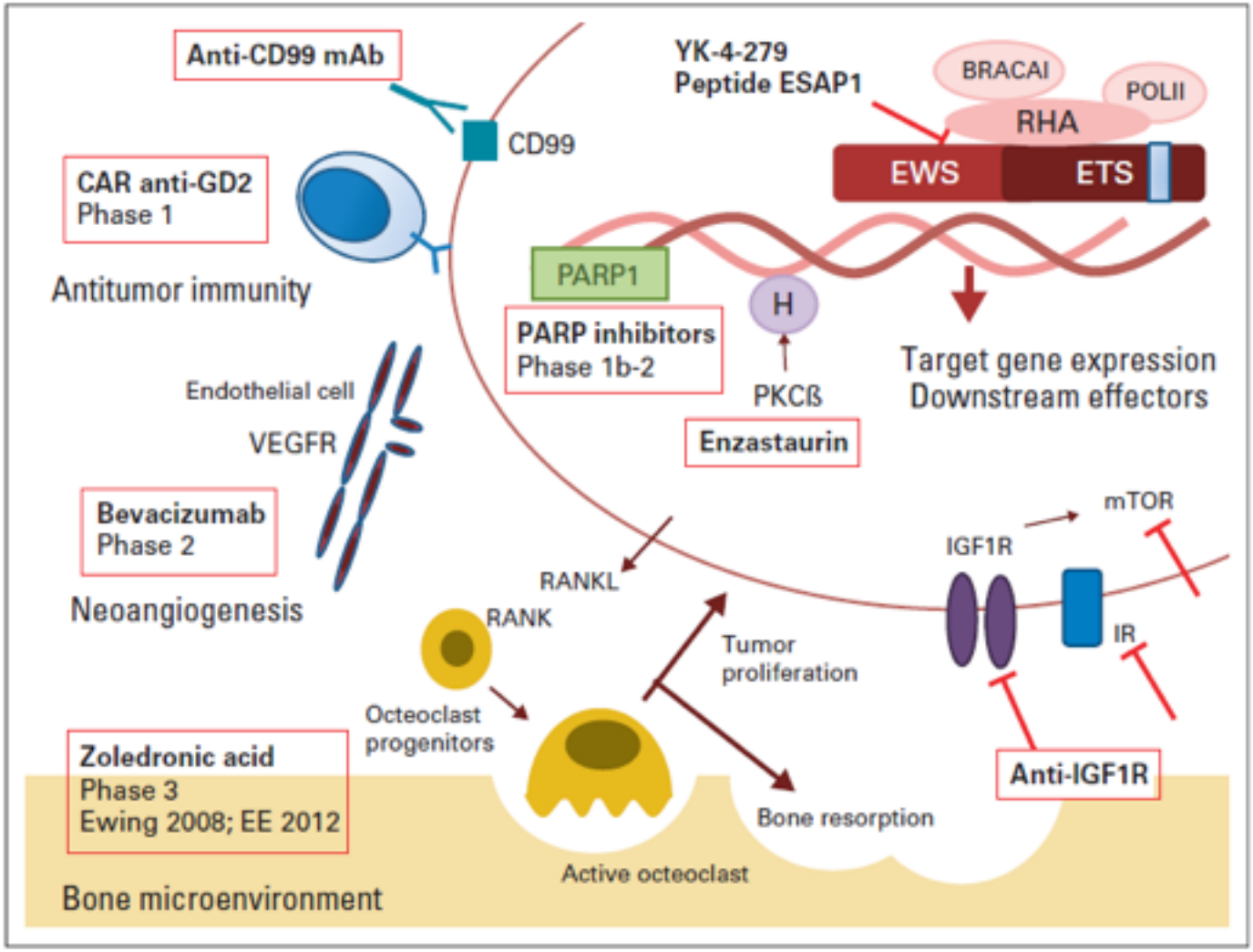
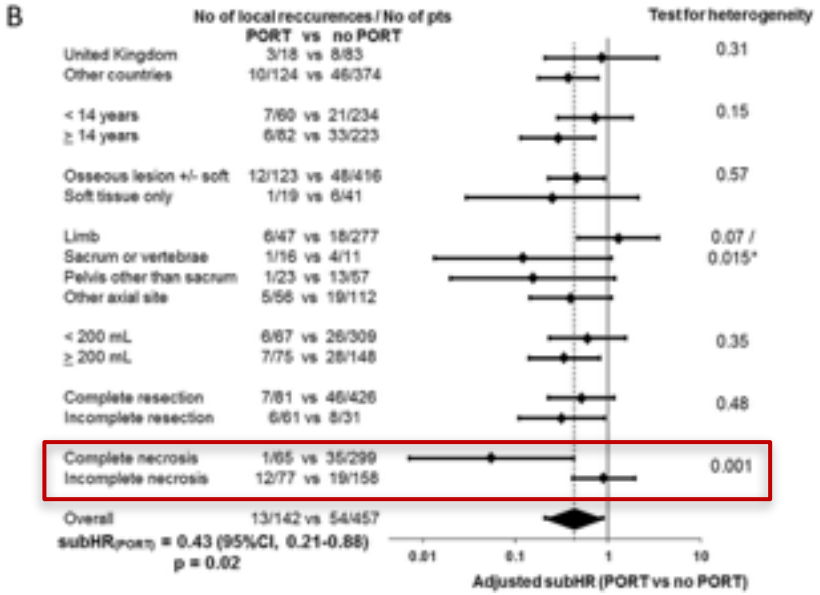


Fig 4. Some new potential targets in Ewing sarcoma. CAR, chimeric receptor gene-modified T cell; EE 2012, Euro-Ewing 2012; H, histone; IGF1R, insulin-like growth factor receptor-1; mAb, monoclonal antibody; mTOR, mammalian target of rapamycin; PARP, poly (ADP-ribose) polymerase; PKC, protein kinase C; RANKL, RANK ligand; RHA, RNA helicase; VEGFR, vascular endothelial growth factor receptor.

➔ European interdisciplinary Ewing sarcoma research summit!

Ewing Sarcoma : Local radiotherapy



Can postoperative radiotherapy be omitted in localised standard-risk Ewing sarcoma? An observational study of the Euro-E.W.I.N.G group

Stéphanie Foulon [a,b], Bernadette Brennan [c], Nathalie Gaspar [d], Uta Dirksen [e], Lee Jeys [f], Anna Cassoni [g], Line Claude [h], Beatrice Seddon [i], Perrine Marec-Berard [j], Jeremy Whelan [g], Michael Paulussen [k,l], Arne Streitbuerger [m], Odile Oberlin [d], Heribert Juergens [e], Robert Grimer [f], Marie-Cécile Le Deley [a,b,*]

S. Foulon et al. / European Journal of Cancer 61 (2016)

RESULTS :

- ➔ 599 patients included to compare benefit of PORT vs non-PORT (retrospective study)
- ➔ 24% with PORT (median dose : 45 Gy)
- ➔ LR-incidence = 11.9%
- ➔ The benefit of PORT was particularly marked for :
  - tumour >200mL at diagnosis
  - 100% necrosis

CONCLUSION : Radiotherapy appears to improve local control. Further studies are required to assess the balance between benefit and risks (see EE2012 Trial).

Take Home Messages…

Osteosarcomas :

- **No benefits from the addition :**
  - of **IE after MAP** (EURAMOS-1) in poor responders
  - of **zoledronic acid** to CT (OS 2006) or **IFN-α-2B** as consolidation treatment (EURAMOS-1)
  - of API-AI vs MTX (OS 2006)

Ewing sarcoma :

- Biomolecular studies involvement ! (new targets)
- Benefit from systematic PORT (except if «ghost-chir.»)
- Benefit from HD CT for localised HR patients
- EE2012 amendment (sept 2016) ➔ BUMEL for R2loc

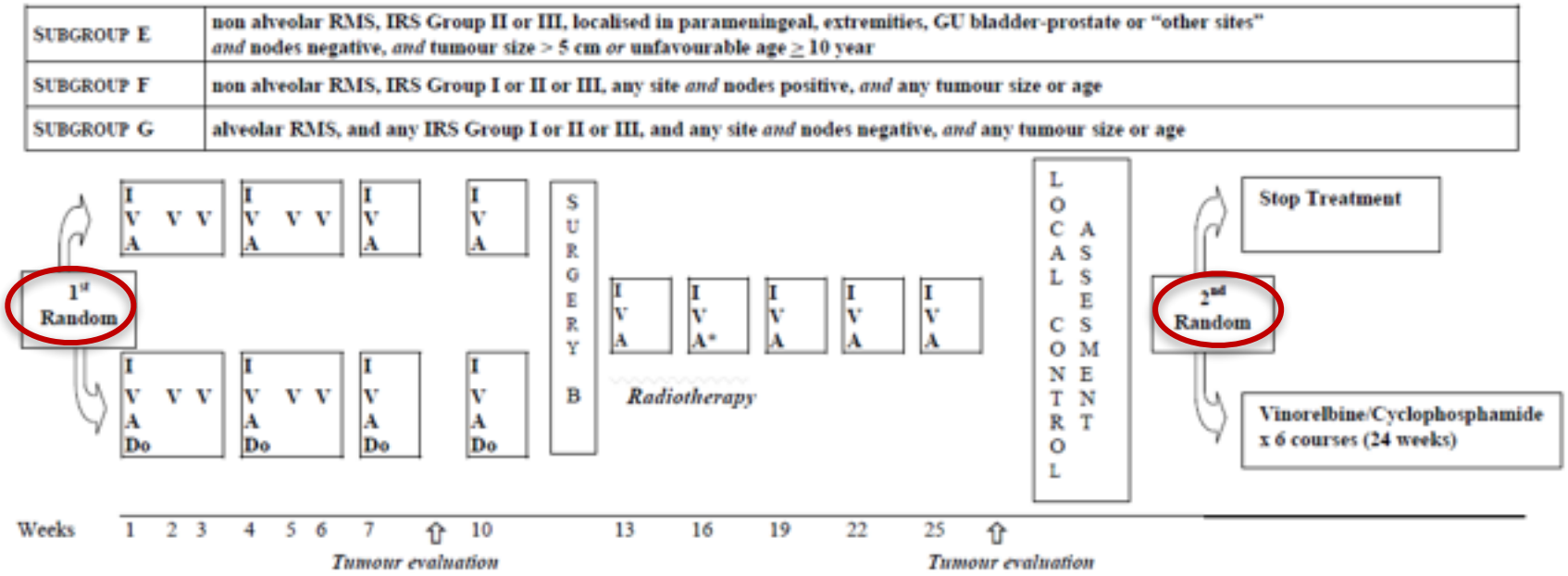
= 15% of patients !

SOFT TISSUE SARCOMAS : RHABDOMYOSARCOMAS (RMS)

RMS : latest results

RMS 2005

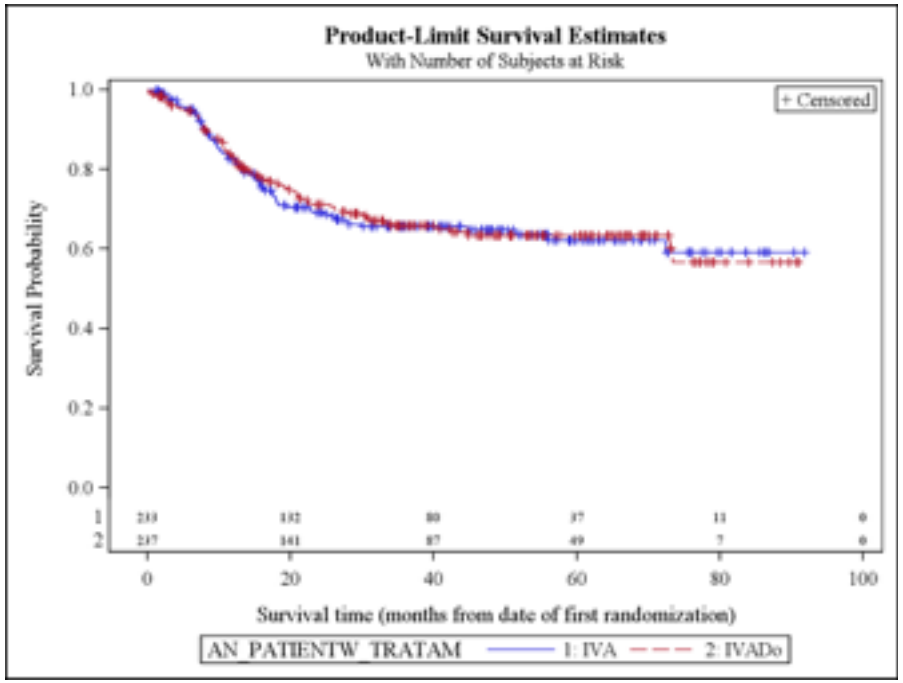
- Protocol for non-metastatic rhabdomyosarcoma
- 4 main groups (Low-Risk – Standard Risk – High Risk – Very High Risk)
- 2 randomisations for **High Risk patients :** IVA vs IVADo/maintenance+/-
  - 3 Sub-groups based on the site, IRS, Nodes, Tumour Size, Patient's age,…



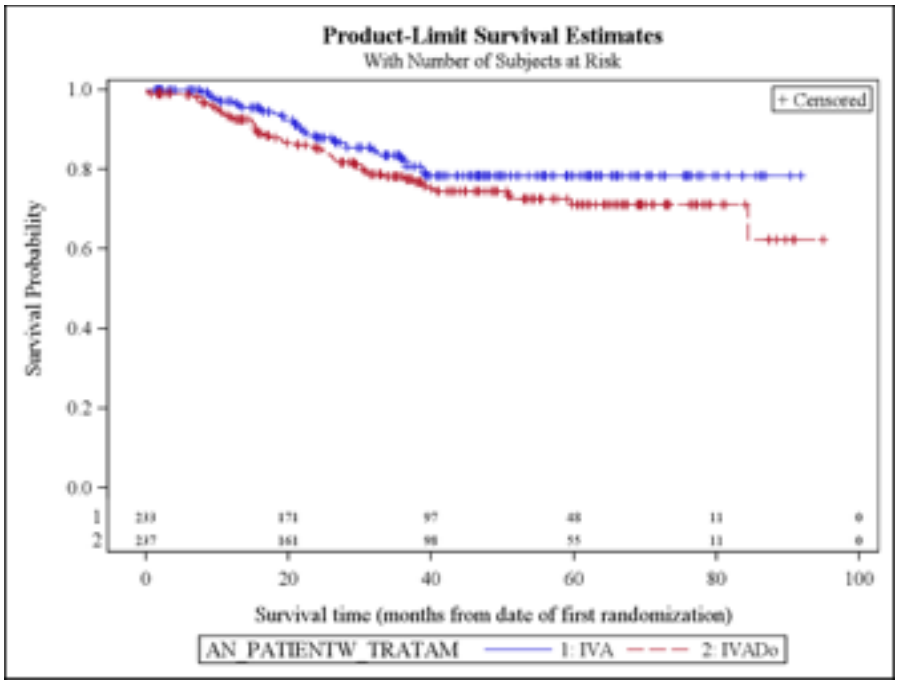
RMS : latest results

RMS 2005 : response to first randomisation

Event Free Survival



Overall Survival



- ➔ Results showed no difference in EFS or OS between the two arms
- ➔ IVA still the standard treatment for localised RMS
- ➔ Randomisation #2 still ongoing (with or without maintenance)

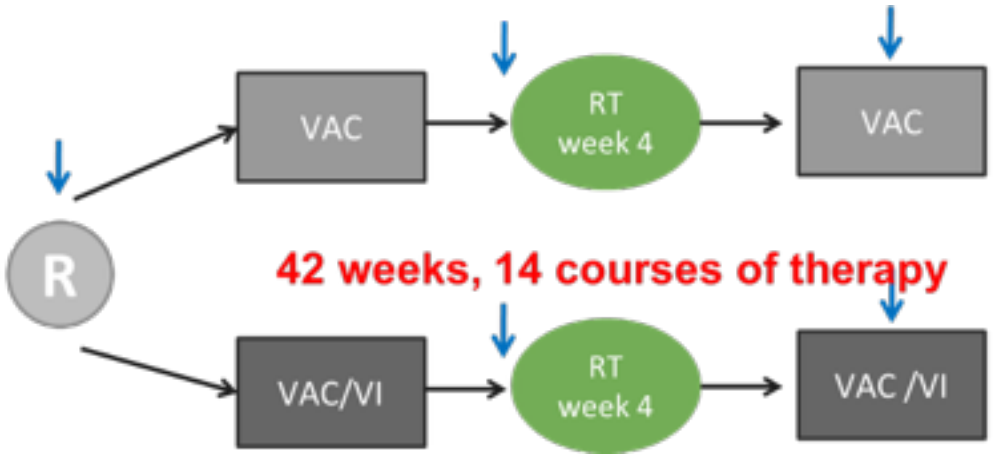
RMS : latest results

COG : ARST0531 Study

TRIAL FEATURES
- Randomisation VAC vs VAC/VI
- Lower CPM dose (1.2 vs 2.2 g/m²)

PRIMARY AIM
- Compare early response rate, EFS, and OS of VAC vs. VAC/VI.

SECONDARY AIM
- Compare EFS, local control, and OS with early RT (week 4) to IRS-IV (week 10).
- Compare early and late effects of VAC vs VAC/VI
- Compare EFS by FDG PET response at weeks 4 and 15
- For VAC/VI patients, compare VI toxicity by UGT1A1 genotype
- Compare VAC toxicity by CYP2B6, CYP2C9 and GSTA1 genotype
- To evaluate and validate gene expression values to define the best predictors and classifiers



Opened December 2006
Closed December 2012

Optional FDG-PET, weeks 1, 4, 15

RMS : latest results

COG : ARST0531 Study Design

TRIAL FEATURES
- Randomisation VAC vs VAC/VI
- Lower CPM dose

PRIMARY AIM
- **Compare early response rate, EFS, and OS of VAC vs. VAC/ VI.**

SECONDARY AIM
- Compare EFS, local control, and OS with early RT (week 4) to IRS-IV (week 10).
- Compare early and late effects of VAC vs VAC/VI
- Compare EFS by FDG PET response at weeks 4 and 15
- For VAC/VI patients, compare VI toxicity by UGT1A1 genotype
- Compare VAC toxicity by CYP2B6, CYP2C9 and GSTA1 genotype
- To evaluate and validate gene expression values to define the best predictors and classifiers

Addition of VI to VAC did not improve outcome for IR-RMS patients but it lowers the hematologic/infectious complications.

➔ VAC/VI treatment is now standard of care in COG treatment strategy to lower alkylating agents doses.

RMS : latest results

COG : ARST0531 Study Design

TRIAL FEATURES

- Randomisation VAC vs VAC/VI
- Lower CPM dose (1.2 vs 2.2 g/m²)

PRIMARY AIM

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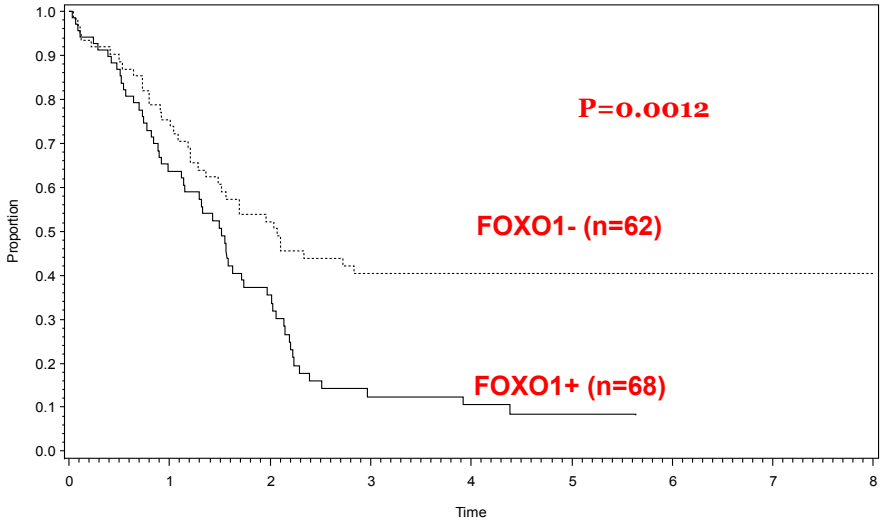
- **To evaluate and validate gene expression values to define the best predictors and classifiers**

PAX/FOXO1 predicts outcome: High-risk (D9802/ARST0431)



Rudzinski E, manuscript under development : FOXO1+ lower OS

OS of patients in HR group with FOXO1+ is worse

RMS : latest results

COG : ARST0531 Study Design

TRIAL FEATURES
- Randomisation VAC vs VAC/VI
- Lower CPM dose (1.2 vs 2.2 g/m²)

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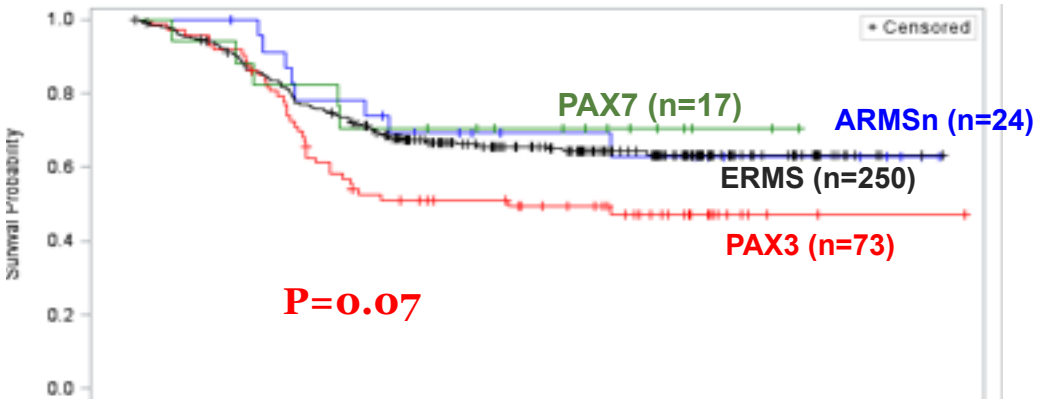
***PAX3-7/FOXO1* predicts outcome: Stage 2/3, Group III only (ARST0531)**



➢ *Skapek SX, Pediatr Blood Cancer 2013; 60:1411-1417 (stage 2/3, Group III)*

➢ *Arnold M, Pediatr Blood Cancer 2016; 63 :634-639 (Low Risk)*

- **76%** of non-metastatic ARMS are *FOXO1*+
  - ➢ *FOXO1* status determined in 80%
  - ➢ Technical failure in 4%
- For Stage 2/3, Group III, *PAX* matters:
  4 year EFS = **49.4%** for ***PAX3/FOXO1***
  4 year EFS = **70.6%** for ***PAX7/FOXO1***

RMS : latest results

BERNIE

Open-label, randomized, phase II study of bevacizumab plus chemotherapy in pediatric metastatic rhabdomyosarcoma (RMS) and non-rhabdomyosarcoma soft tissue sarcoma (NRSTS)

An academic-industry (ROCHE) collaboration for new drug development in pediatric STS

PRIMARY OBJECTIVES :

- Evaluate EFS with/without bevacizumab addition

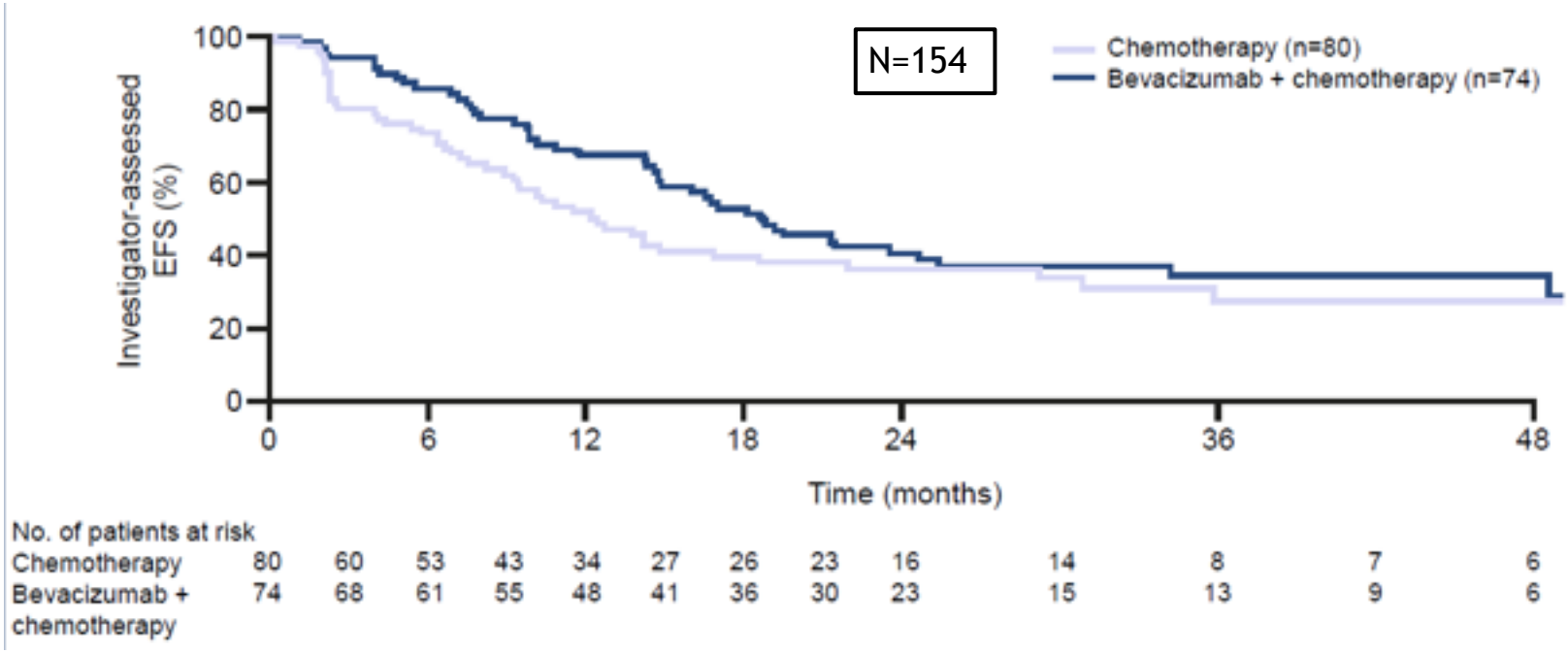
SECONDARY OBJECTIVES :

- Evaluation of safety, tolerability and efficacy when addition of bevacizumab compared to chemotherapy alone
- Characterization of pharmacokinetic profile of bevacizumab across all age subsets of the study population
- Correlation of biomarker assessments with risk factors and treatment outcome

RMS : latest results

BERNIE

Open-label, randomized, phase II study of bevacizumab plus chemotherapy in pediatric metastatic rhabdomyosarcoma (RMS) and non-rhabdomyosarcoma soft tissue sarcoma (NRSTS)



- ➢ No significant improvement with the addition of bevacizumab to standard treatment
- ➢ Clinically meaningful improvement of objective response rate (long-term OS FU continues)
- ➢ No enhanced toxicity compared to the adults

SOFT TISSUE SARCOMAS :
NON-RHABDO SOFT TISSUE SARCOMAS (NRSTS)

Non-RMS Tumours : update

DESMOID TUMORS (ORBACH, EpSSG meeting 2016)

- **Not a so rare disease**:
  - 163 pts (184 SS in NRSTS 05 – 12/2015)
  - Lack of recruitment nevertheless
- **Large prospective series**:
  - [Meazza 2010 - 94 pts; Oudot 2012 - 57 pts; Soto-Miranda 2013 - 39 pts]
- **Difficult disease with many different events**: regression, progression, relapse …
- **Different from adults**:
  - Few Trauma
  - Few genetic APC association … (but all analyzed ?)
  - Less mesenteric primaries

ABSTRACT SIOP MEETING 2016

DESMOID TUMORS IN CHILDREN: THE EXPERIENCE OF THE EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA GROUP (EpSSG)

Authors: Daniel Orbach, Julia Daragjati, Max Van Noesel, Bernadette Brennan, Véronique Minard-Colin, Gianni Bisogno, Nadege Corradini, Meriel Jenney, Gian Luca De Salvo, Anne Sophie Defachelles, Anna Kelsey, Myriam Ben Arush, Nadine Francotte, Andrea Ferrari.

Non-RMS Tumours : update

original article

Annals of Oncology 26: 567–572, 2015

Synovial sarcoma in children and adolescents: the European Pediatric Soft Tissue Sarcoma Study Group prospective trial (EpSSG NRSTS 2005)

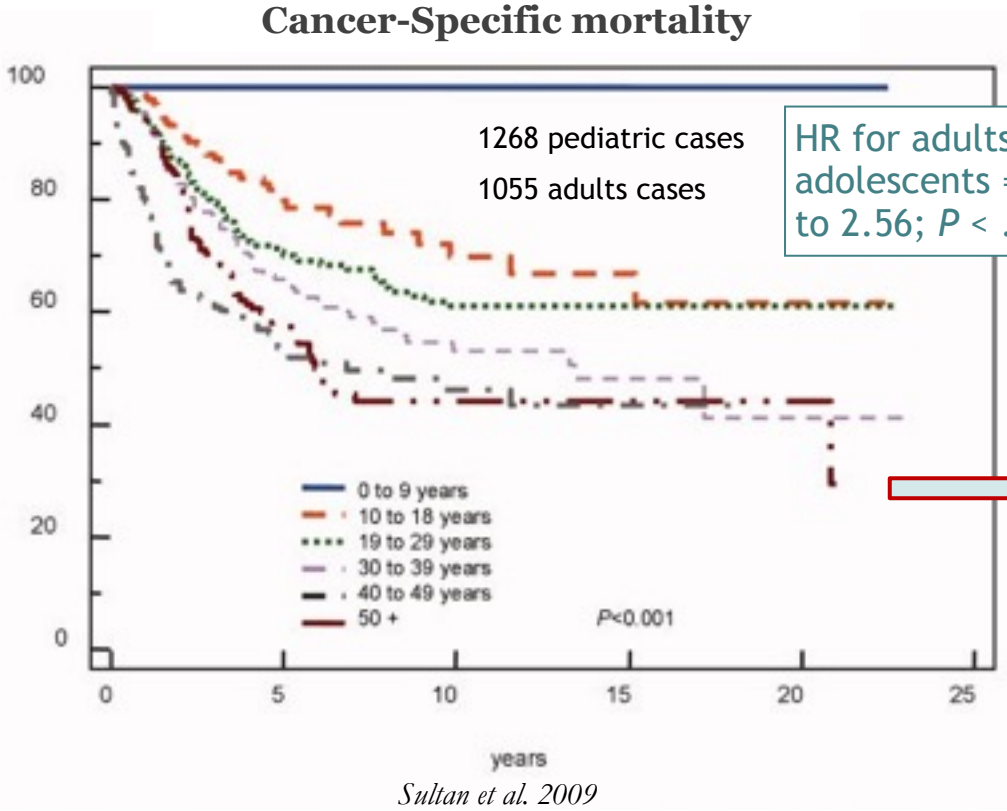
A. Ferrari[1*], G. L. De Salvo[2], B. Brennan[3], M. M. van Noesel[4], A. De Paoli[2], M. Casanova[1], N. Francotte[5], A. Kelsey[6], R. Alaggio[7], O. Oberlin[8], M. Carli[9], M. Ben-Arush[10], C. Bergeron[11], J. H. M. Merks[12], M. Jenney[13], M. C. Stevens[14], G. Bisogno[9] & D. Orbach[15]

- 138 patients <21y with non-metastatic synovial sarcoma
- 3-years EFS = 81.9% / OS = 97.2% - 5-years EFS = 80.7% / OS = 90.7%
- Risk group stratification gives a prognostic value
- Need for a larger, international project

Non-RMS Tumours : update

SYNOVIAL SARCOMA (ORBACH, EpSSG meeting 2016)

- ➢ New « SYNO BIO Study » : predictive tool for metastatic outcome in children and adolescents with synovial sarcoma.
- ➢ Difference between adult and pediatric synovial sarcoma



Sultan et al. 2009

HR for adults vs children/ adolescents = 2.52, 95% CI = 1.56 to 2.56; *P* < .001

Worse outcome in adult compared to pediatric cases, but why? (Biological/treatment differences?)

SOFT TISSUE SARCOMAS :
INFANTILE FIBROSARCOMA

Infantile Fibrosarcoma : papers

Conservative strategy in infantile fibrosarcoma is possible: The European paediatric Soft tissue sarcoma Study Group experience

Daniel Orbach [a,*], Bernadette Brennan [b], Angela De Paoli [c], Soledad Gallego [d], Peter Mudry [e], Nadine Francotte [f], Max van Noesel [g], Anna Kelsey [h], Rita Alaggio [i], Dominique Ranchère [j], Gian Luca De Salvo [c], Michela Casanova [k], Christophe Bergeron [l], Johannes H.M. Merks [m], Meriel Jenney [n], Michael C.G. Stevens [o], Gianni Bisogno [p], Andrea Ferrari [k]

- Infantile fibrosarcoma (IFS) = rare disease
- Compliance of European countries permit the achievement of a standardized treatment
- Conservative treatment doesn't jeopardize survival
- VA regimen should be the first line therapy

Pediatr Blood Cancer 0000;00:000–000

BRIEF REPORT

Infantile Fibrosarcoma With *NTRK3–ETV6* Fusion Successfully Treated With the Tropomyosin-Related Kinase Inhibitor LOXO-101

Ramamoorthy Nagasubramanian, MD,[1]* Julie Wei, MD,[1] Paul Gordon, MD,[1] Jeff C. Rastatter, MD,[2] Michael C. Cox, Pharm.D., MHSc,[3] and Alberto Pappo, MD[4]

- Pediatric patient with refractory IFS (ETV6-NTRK3 fusion+)
- Treated with an oral pan-TRK inhibitor (LOXO-101), a TRK targeting IMP
- 90% of tumor regression after one month – CR after 2 months

MAPPYACT study : systematic detection of NTRK3-ETV6 transcript and potential therapeutic targeting

Take Home Messages…

RMS :

- **COG**
  - PAX3/FOXO1 fusion associated with poor prognosis (IR)
  - VI/VAC treatment as standard to lower alkylating agents doses
- **No benefits from adding**
  - Doxo for localised HR patients (RMS2005)
  - Bevacizumab for metastatic STS patients (BERNIE)
- **RMS2005** <21 years → second randomisation ongoing (+/- 6-month maintenance therapy for HR patients).
- **AYA :** Systematic assignement of AYA in HR groups

NRSTS :

- Biomolecular studies ! (NTRK-ETV6 prognosis, new drugs, new targets, …)
- Synovial sarcoma: Good results with EpSSG strategy
- Infantile fibrosarcoma: Role of conservative treatment

Thank you for your attention !