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complex diseases

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Paediatric Cancer  
(ERN PaedCan)



*October 20<sup>th</sup> 2021*

*Daniela Di Carlo & Andrea Ferrari*

*“A challenging case of  
Rhabdomyosarcoma...”*

*Chair: Teresa De Rojas*

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# COI Declaration

## No conflict of interest to declare



# Onset of symptoms

- 6-yrs old girl presenting with back pain extended to the right leg
- Worsening pain till acute paraplegia
- MRI: mass in appearance centered on spinal process of D7, from D6 to D8, epidural extension, spinal cord compression + multiple vertebral lesions (from D6 to S2)



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# What would you suspect?

- Ewing sarcoma
- Neuroblastoma
- Soft tissue sarcoma
- Large B-cell lymphoma



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# What would you do?

- Biopsy of the lesion + start of disease-specific chemotherapy
- Urgent start of chemotherapy
- Laminectomy + biopsy



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# What has been done

- Urgent decompressive laminectomy + gross resection of the epidural mass



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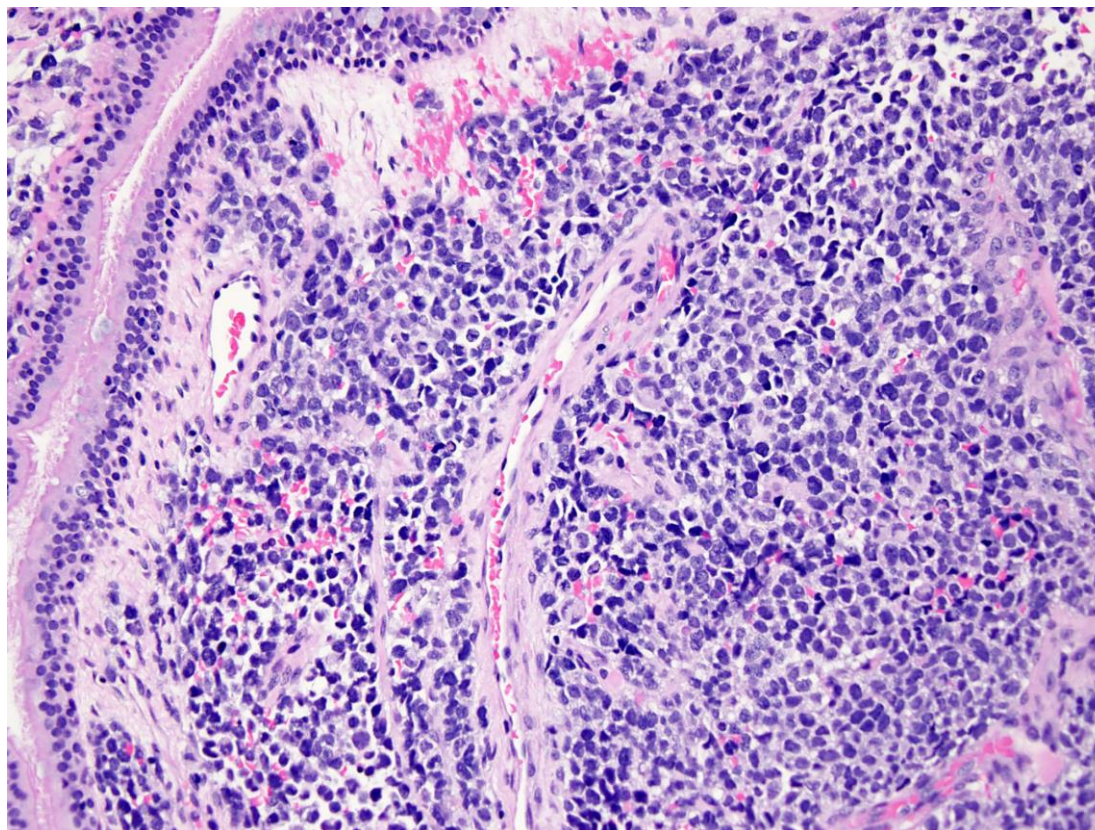
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# Histopathology

## Alveolar RMS, t(2;13), PAX3-FOXO1

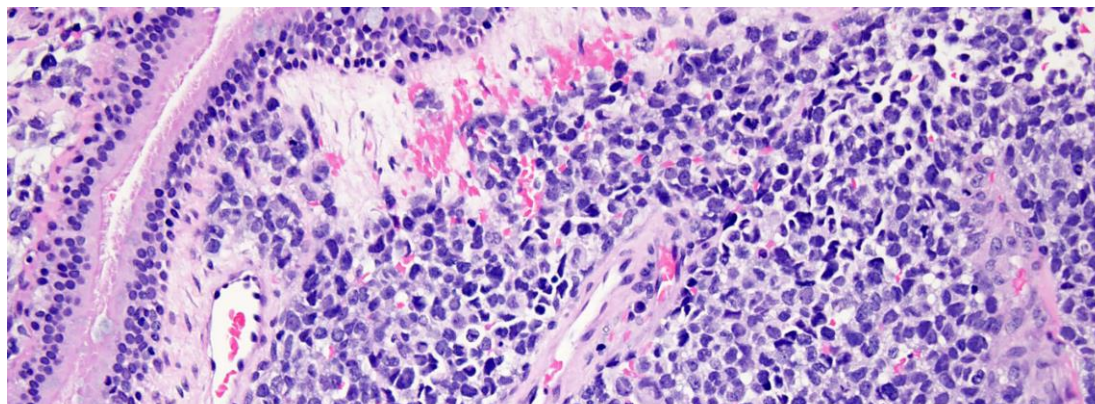






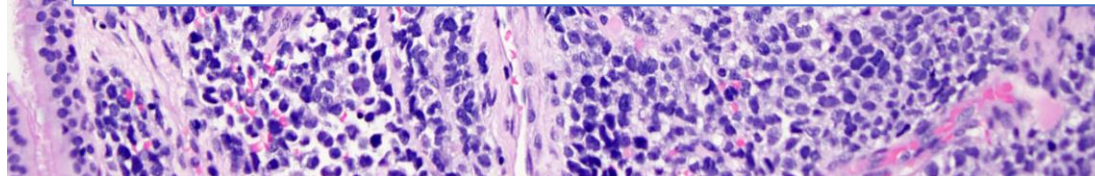
# Histopathology

## Alveolar RMS, t(2;13), PAX3-FOXO1



### Bullet points!

- Soft tissue sarcoma = rare cause of cord compression!
- Spinal compression = real emergency!
- Urgent laminectomy and decompression are suggested!







# Histopathology

Alveolar RMS, t(2;13), PAX3-FOXO1





# Staging

- . PET-MRI: thecal, paravertebral lesions, lesions at the sternum, left iliac bone, right and left femur, right tibia, soft tissues of the right leg
- . CNS-spinal MRI: sphenoidal clivus lesion
- . CT scan: lesion 8th rib
- . MRI of the right leg: soft mass in gastrocnemius muscle
- . Bone marrow smears: POS
- . Osteo-medullar biopsies: POS



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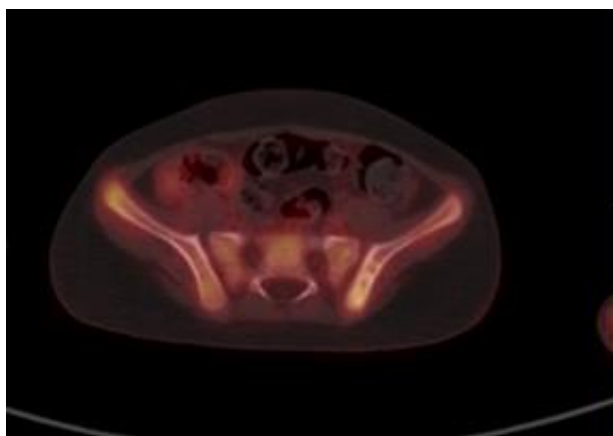
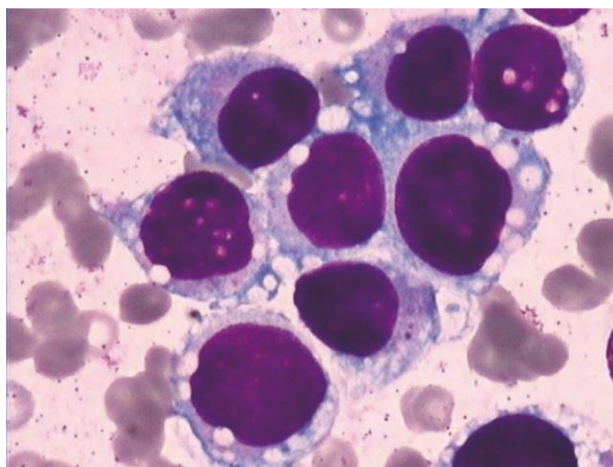


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# Staging





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# The final diagnosis

Alveolar RMS, t(2;13) → PAX3-FOXO1

Primary site: gastrocnemius muscle

Metastasis: osteo-medullar sites



# The final diagnosis

Alveolar RMS, t(2;13) → PAX3-FOXO1

Primary site: gastrocnemius muscle

Metastasis: osteo-medullar sites



## Bullet points!

- Molecular diagnosis is now routinely used for the stratification of the patients in risk groups!
- Classical fusions: PAX3-FOXO1 t(2;13) or PAX7-FOXO1 t(1;13)
- Fusion positive vs Fusion negative
- Fusion positive = worse outcome



# What has been done

## 3 x IrIVA

- ↓ captation PET
- = volume MRI
- Bone Marrow +





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# Bullet point: IrIVA!

**TJ Tumori Journal**

Short Communication

**Multiagent chemotherapy including IrIVA regimen and maintenance therapy in the treatment of desmoplastic small round cell tumor**

Andrea Ferrari<sup>1</sup>, Luca Bergamaschi<sup>1</sup>, Stefano Chiaravalli<sup>1</sup>, Emilia Pecori<sup>2</sup>, Barbara Diletto<sup>2</sup>, Ombretta Alessandro<sup>2</sup>, Tommaso Giandini<sup>3</sup>, Livellara Virginia<sup>1</sup>, Giovanna Sironi<sup>1</sup> and Michela Casanova<sup>1</sup>

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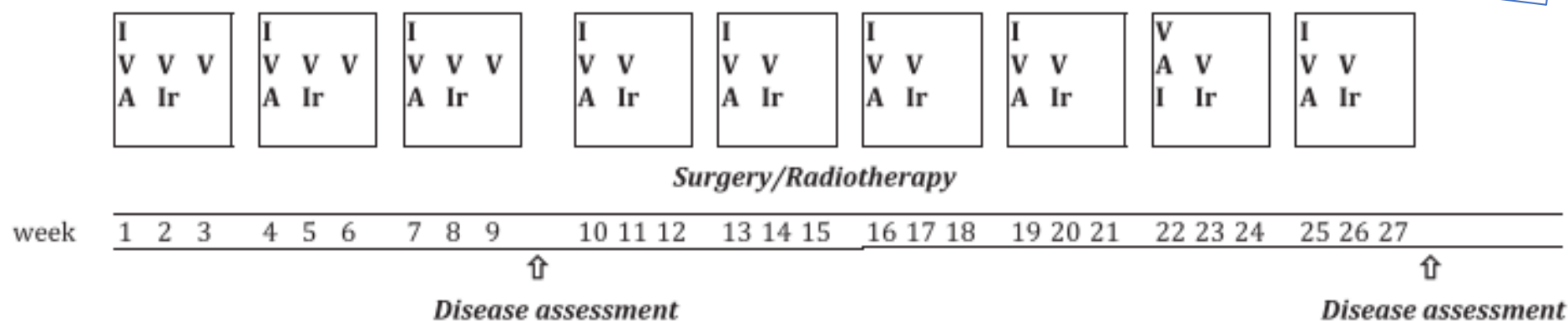
Received: 18 October 2020 | Revised: 13 December 2020 | Accepted: 7 January 2021  
DOI: 10.1002/pbc.28951

**ONCOLOGY: RESEARCH ARTICLE**

**Integrating irinotecan in standard chemotherapy: A novel dose-density combination for high-risk pediatric sarcomas**

anni Bisogno<sup>1</sup>, Andrea Ferrari<sup>2</sup>, Arianna Tagarelli<sup>3</sup>, Stefano Chiaravalli<sup>2</sup>, Elena Poli<sup>1</sup>, Giovanni Scarzello<sup>4</sup>, Silvia Sorbara<sup>3</sup>, Michela Casanova<sup>2</sup>, Maria Carmen Affinita<sup>3</sup>, Federica De Corti<sup>5</sup>

Pediatric Blood & Cancer  
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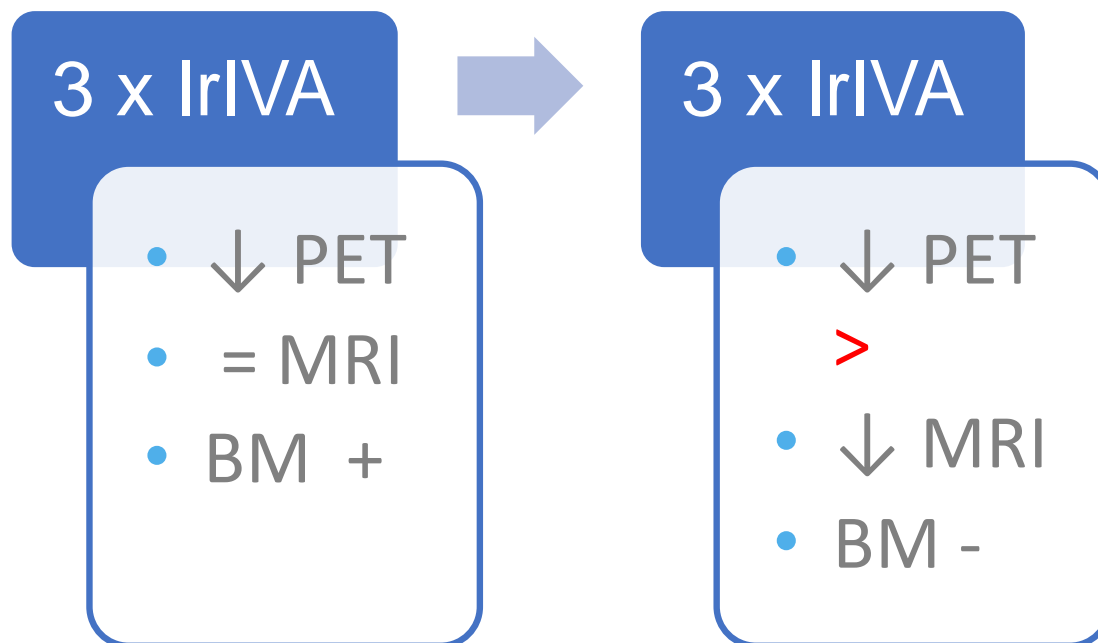
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# What has been done



!! Reduction in signal at PET > MRI

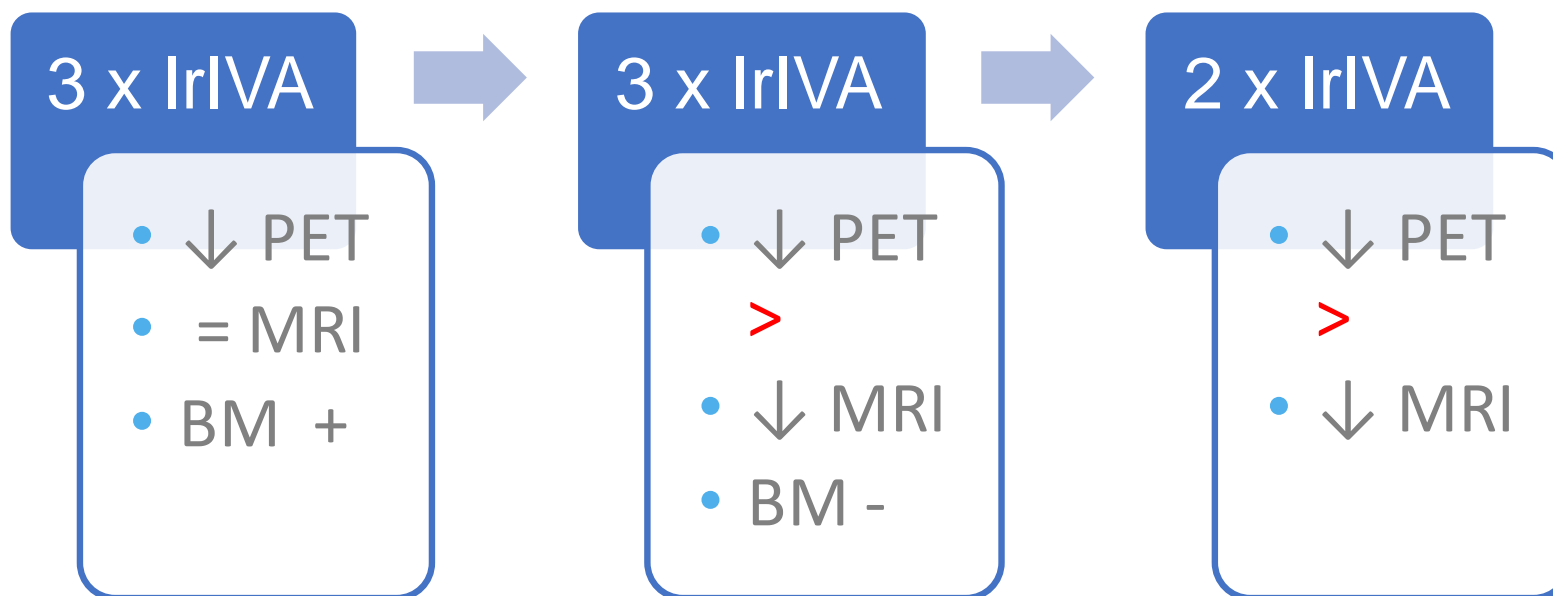


# What would you do?

- **Surgery** on the primary site + Chemo + RT on **all** positive lesions **at diagnosis**
- Chemo + RT on **all** positive lesions **at diagnosis** (no surgery)
- Chemo + RT on all lesions still positive **after 6 cycles of chemo**
- Chemo + new tumor response evaluation to decide irradiation sites (after 8-9 cycles)



# What has been done



!! Reduction in signal at PET > MRI



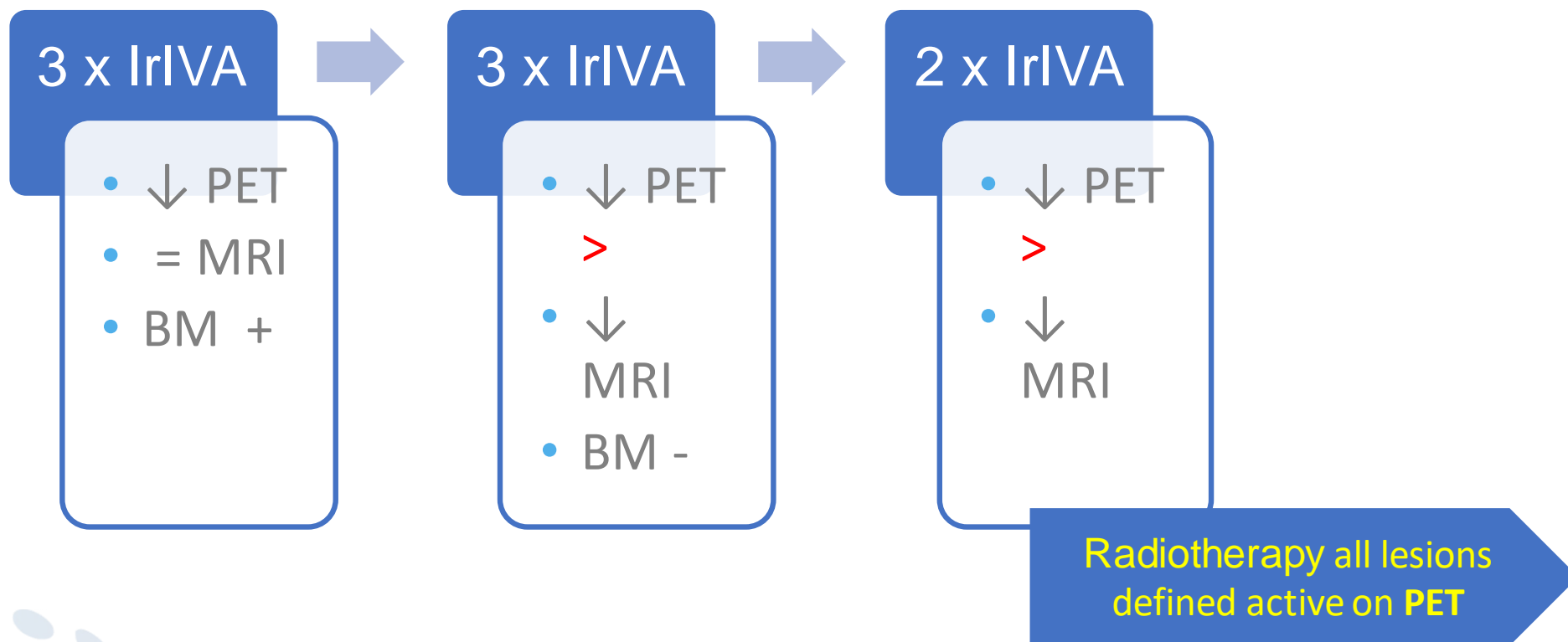
# We do need irradiation but...

- of **all** positive lesions **at diagnosis**?
- of all lesions **still** positive at PET after 8 cycles?
- of all lesions **still** positive at MRI after 8 cycles?






# What has been done






# Bullet point: PET-scan!

**ELSEVIER**

journal homepage: [www.ejcancer.com](http://www.ejcancer.com)



Original Research

Role of  $^{18}\text{F}$ -FDG-PET/CT in the staging of metastatic rhabdomyosarcoma: a report from the European paediatric Soft tissue sarcoma Study Group

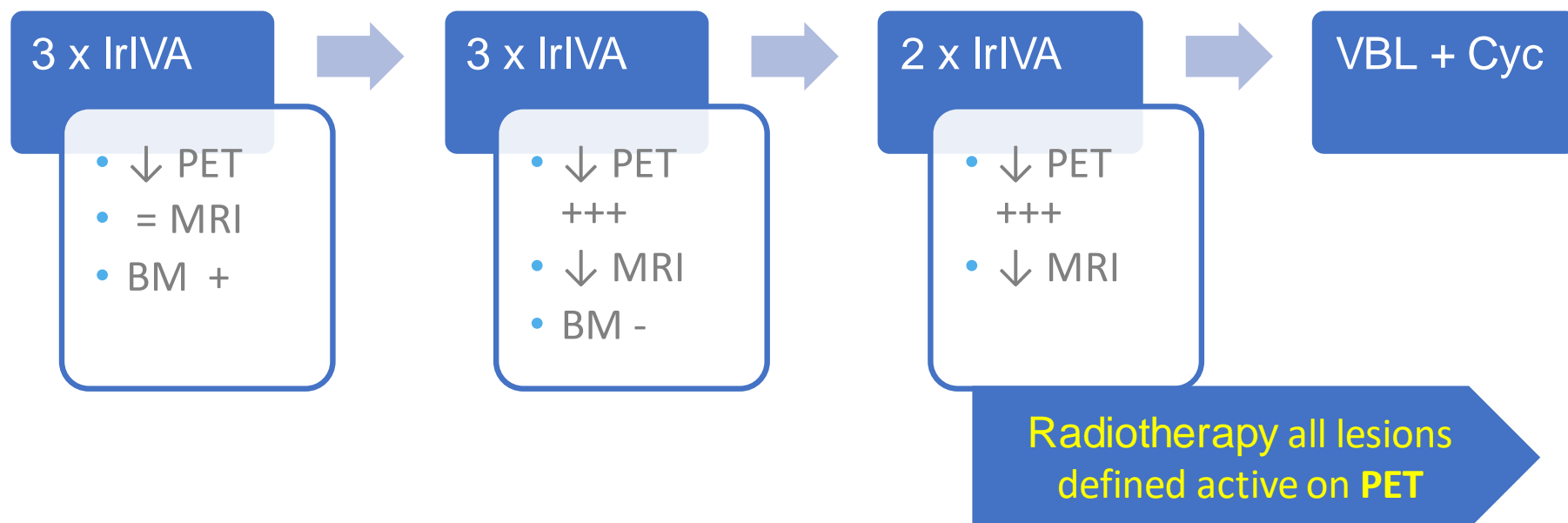
Federico Mercolini <sup>a,\*</sup>, Pietro Zucchetta <sup>b</sup>, Nina Jehanno <sup>c</sup>,  
Nadege Corradini <sup>d</sup>, Rick R. Van Rijn <sup>e</sup>, Timothy Rogers <sup>f</sup>,  
Alison Cameron <sup>g</sup>, Giovanni Scarzello <sup>h</sup>, Beatrice Coppadoro <sup>i</sup>,  
Veronique Minard-Colin <sup>j</sup>, Soledad Gallego <sup>k</sup>, Julia Chisholm <sup>l</sup>,  
J.Hans Merks <sup>m</sup>, Gianni Bisogno <sup>i</sup>

## Bullet points!

- In the previous protocol PET scan was considered optional.
- In the next protocol it will be mandatory and its role will be discussed!



# What has been done





# Bullet point: Maintenance!



## Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial



Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Soledad Gallego Melcón, Johannes H Merks, Anna Kelsey, Helene Martelli, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Ilaria Zanetti, Christine Devalck, Myriam Ben-Arush, Peter Mudry, Sima Ferman, Meriel Jenney\*, Andrea Ferrari\*, for the European paediatric Soft tissue sarcoma Study Group

### Summary

**Background** For more than three decades, standard treatment for rhabdomyosarcoma in Europe has included *Lancet Oncol* 2019

## Bullet points!

- Maintenance therapy = revolution in the treatment of RMS!
- Maintenance therapy improves survival for HR patients!
- Superiority of the experimental arm vs standard arm!
- Proposed also for metastatic patients.



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# Expert time: Andrea Ferrari



# Take-home messages !

- Unknown *versus* metastatic with little primary tumor  
...it is important to perform a complete study of all the limbs.
- Urgent laminectomy: rare event but real emergency!
- IrIVA: dose-density regimen for patients with poor prognosis.
- The role of the PET-scan.
- The role of maintenance for very-high-risk patients.