



# Autologous Hematopoietic Stem Cell Transplantation in patients with high risk Neuroblastoma treated with/without Metaiodobenzylguanidine

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*Mofid Hospital*

*Tehran ,IRAN*

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# Tehran University of Medical Sciences

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# History of Stem Cell Transplantation in HORCSCT



The Hematology-Oncology Research Center and Stem Cell Transplantation (HORCSCT) is affiliated to Tehran University of Medical Sciences (TUMS), Tehran, Iran.



The Center was founded in **1991** by Professor Ghavamzadeh, who is currently the Center director.



# Pediatric Hematopoietic Stem Cell Transplantation Unit

Since **2007** one of SCT wards specialized to children which named Pediatric SCT ward. It had 7 active beds at first, now has 11 active beds.





# Pediatric SCT Unit

- **HORCSCT is among the most prominent stem cell transplantation centers in the world, with more than 400 transplantations performed per year.**
- **EACH YEAR MORE THAN 110 HSCT IN PEDIATRIC**



# Pediatric SCT Unit

**From the first days of its activity, it was possible to perform transplantation of all the**

- **Malignant hematologic diseases**
- **Non-malignant hematologic diseases**
- **Solid tumors**
- **Primary Immunodeficiencies**
- **Metabolic diseases**

# Pediatric SCT Unit

- Now in addition, even transplantation of infants less than 4 months is being performed in this section.





# Pediatric SCT Unit

Between 1991 and July 2013

Total : **1160** patients

691 boys , 469 girls

<15 year old

Median age = 8 years ( 4 months -15 years)

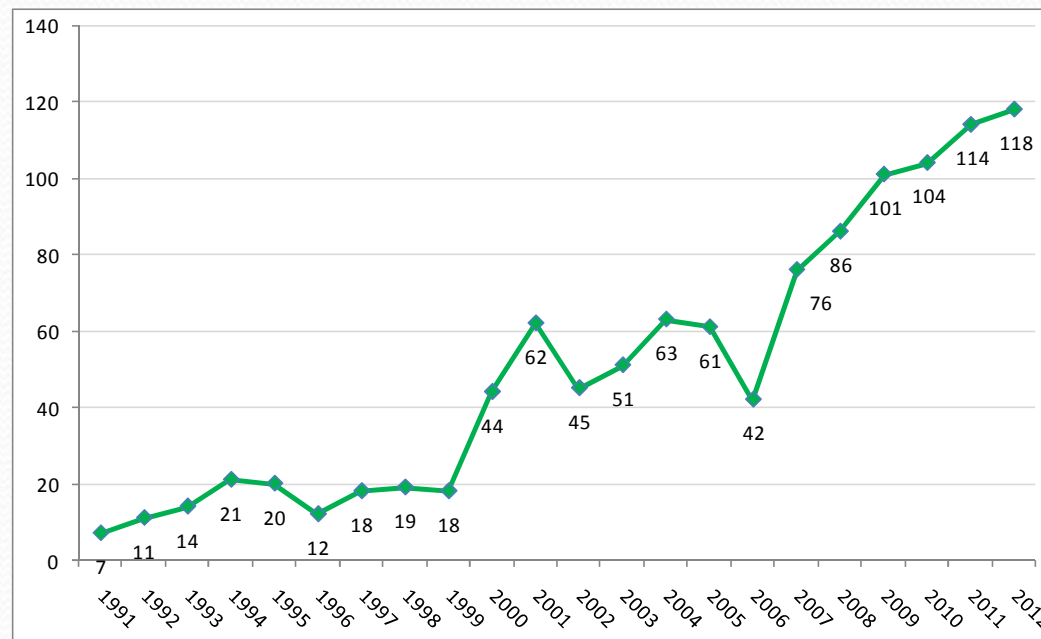
Mean age =  $8 \pm 4.4$



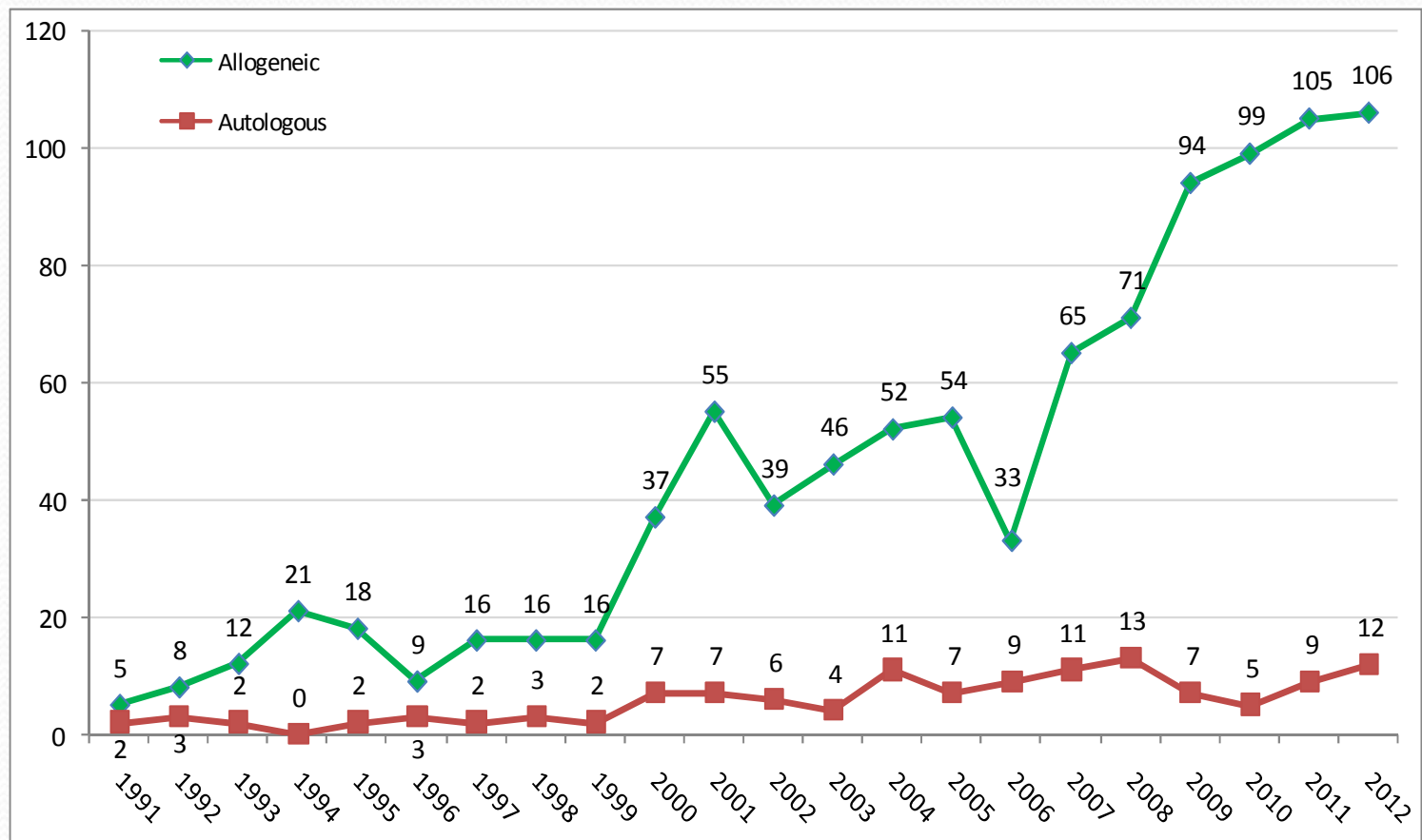




# Pediatric HSCT in IRAN from 1991 till December 2012



# Pediatric HSCT in IRAN from 1991 till December

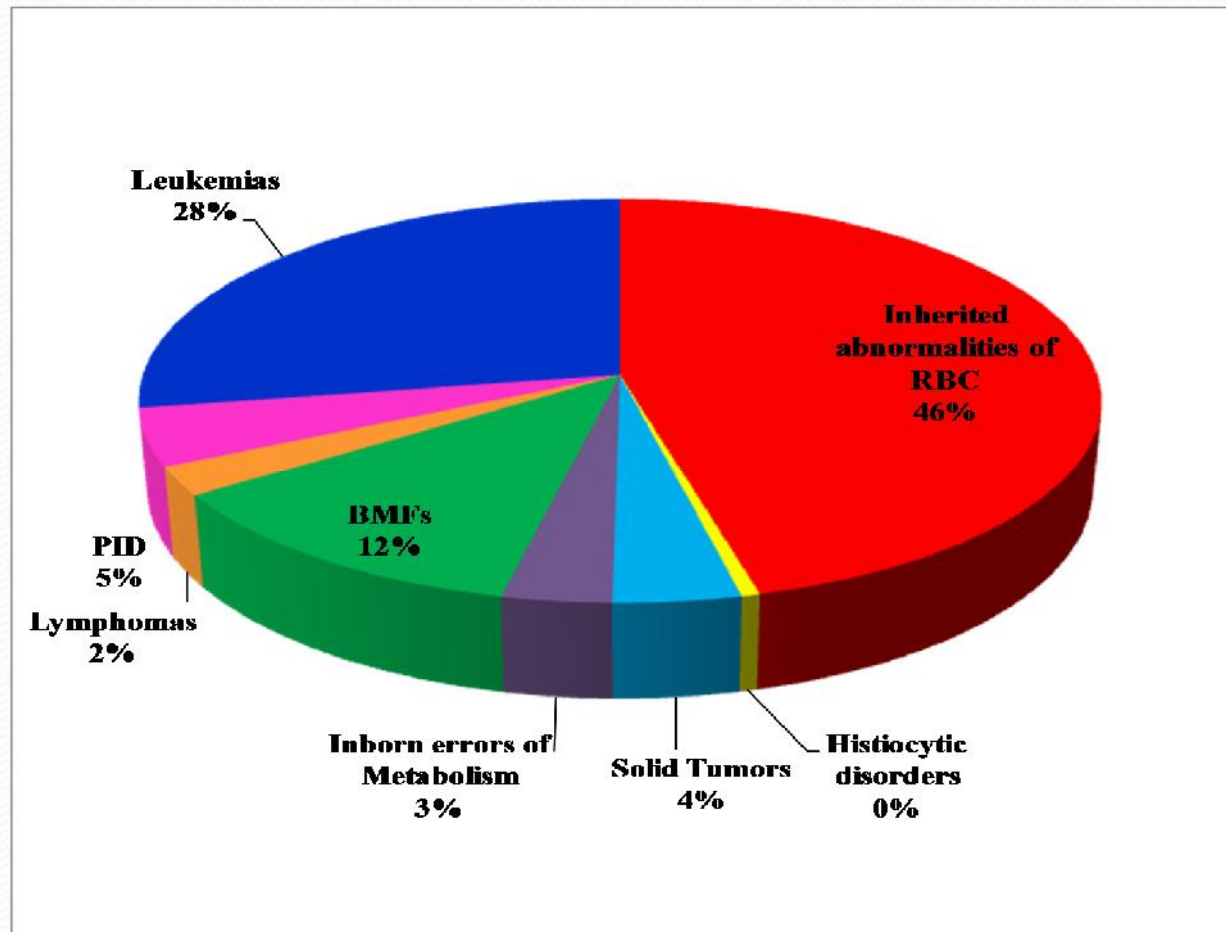




# By Graft

- **Allogeneic** 1028 (88.6%)
- **Autologous** 129 (11.1%)
- **Syngenic**





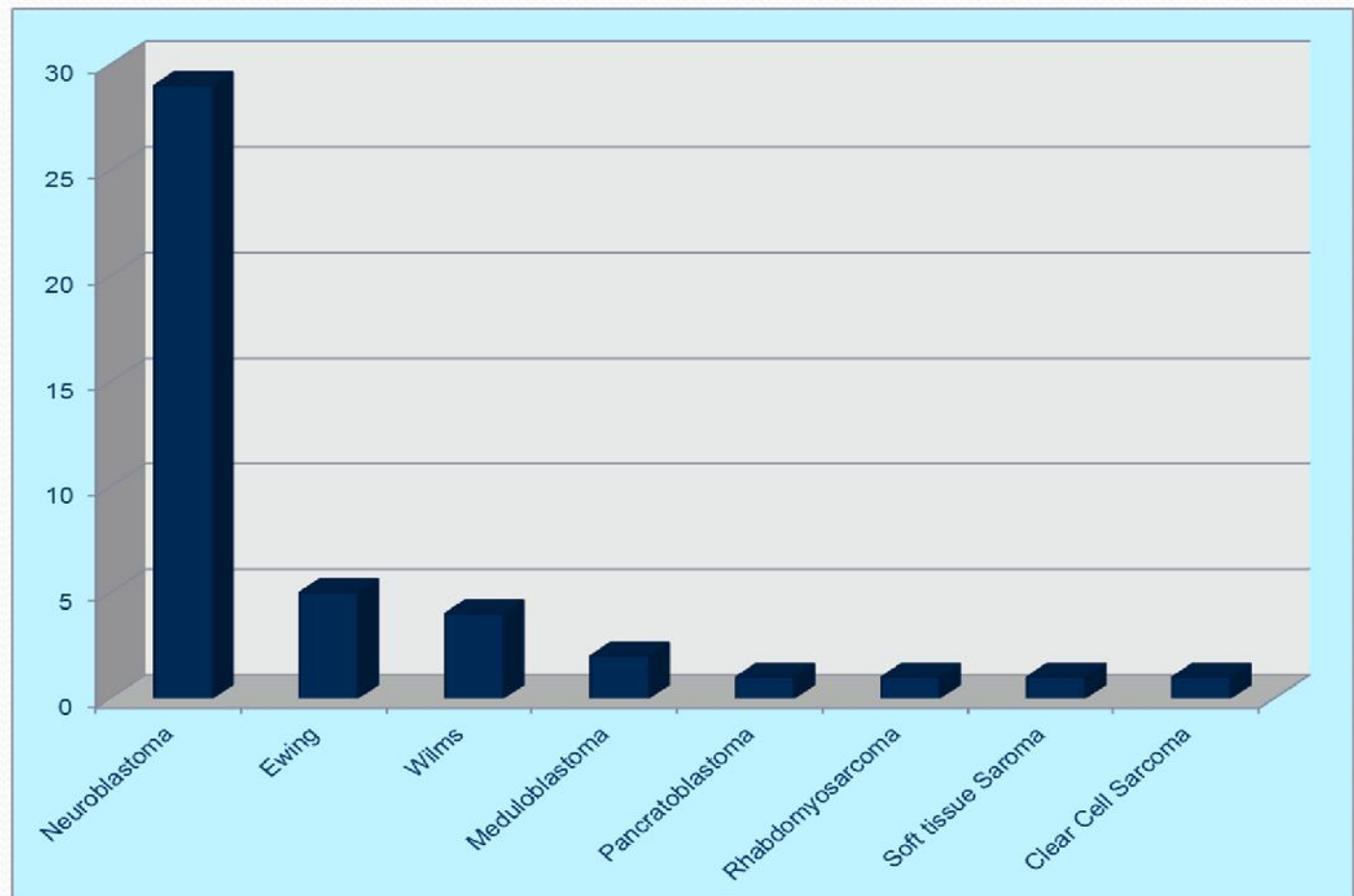


# By Disease

• Inherited abnormalities of RBC	531
• Leukemias and lymphomas	343
• Bone Marrow Failure syndrom	144
• Primary Immunodeficiencies	60
• Solid Tumors	44
• Inborn Errors of Metabolism	38

# Solid Tumors

- 44 (3.7%)





# Introduction

- **Neuroblastoma is the most common extracranial, solid tumor in children**
- **Accounting for 8% to 10% of all childhood cancers.**
- **Approximately 70% of patients have metastatic disease at diagnosis.**



# Risk-based Neuroblastoma Treatment Plan

1. Age at diagnosis
  2. Clinical stage of disease
  3. Tumor histology
  4. Presence of the N-myc
- Risk-based treatment plan assigns each patient to a low-risk, intermediate-risk or high-risk group .





Risk category	Description
Low risk	<ul style="list-style-type: none"> <li>• stage 1 disease</li> <li>• stages 2A and 2B, except for a child age one or older with MYCN amplification and unfavorable histology</li> <li>• stage 4S with no MYCN amplification, favorable histology, and hyperdiploid</li> </ul>
Intermediate risk	<ul style="list-style-type: none"> <li>• stage 3, age less than one year and no MYCN amplification</li> <li>• stage 3, age one or older with no MYCN amplification and favorable histology</li> <li>• stage 4, age less than one year with no MYCN amplification</li> <li>• stage 4S with no MYCN amplification, unfavorable histology, and/or diploid</li> </ul>
High risk	<ul style="list-style-type: none"> <li>• stages 2A and 2B, age one or older, MYCN amplification and unfavorable histology</li> <li>• stage 3 with MYCN amplification</li> <li>• stage 3, age one or older, no MYCN amplification and unfavorable histology</li> <li>• stage 4, age one or older</li> <li>• stage 4, age less than one year with MYCN amplification</li> <li>• stage 4S with MYCN amplification</li> </ul>



# Autologous Hematopoietic Stem Cell Transplantation (HSCT)

- According to the NCI (2008),  
  
autologous HSCT is listed as a standard treatment option for individuals classified as having high-risk disease.
- Berthold, 2005; Matthay, 1999  
Ladenstein, 2008; Zage, 2008;  
Trahair, 2007; Vedeguer, 2004

# Background

- The aim of this study is to compare two main strategies of auto-HSCT for patients with high risk Neuroblastoma
  1. Auto-HSCT alone in patients with negative diagnostic MIBG
  2. Auto-HSCT with therapeutic MIBG before HSCT in patients with positive diagnostic MIBG.



# Methods

- We prospectively analyzed the outcome of 20 patients ( 9 girls , 7 boys) with high risk Neuroblastoma who had undergone auto-HSCT between May 2007 and December 2012.
- Median age at transplantation was 5.1 years.

# Methods

- According to the results of diagnostic MIBG, patients were divided into two groups:
  - MIBG-avid (n=10)
  - non MIBG-avid (n=10)
- MIBG-avid patients received  $^{131}\text{I}$ -MIBG (12mci/kg) on day 21 before transplantation.



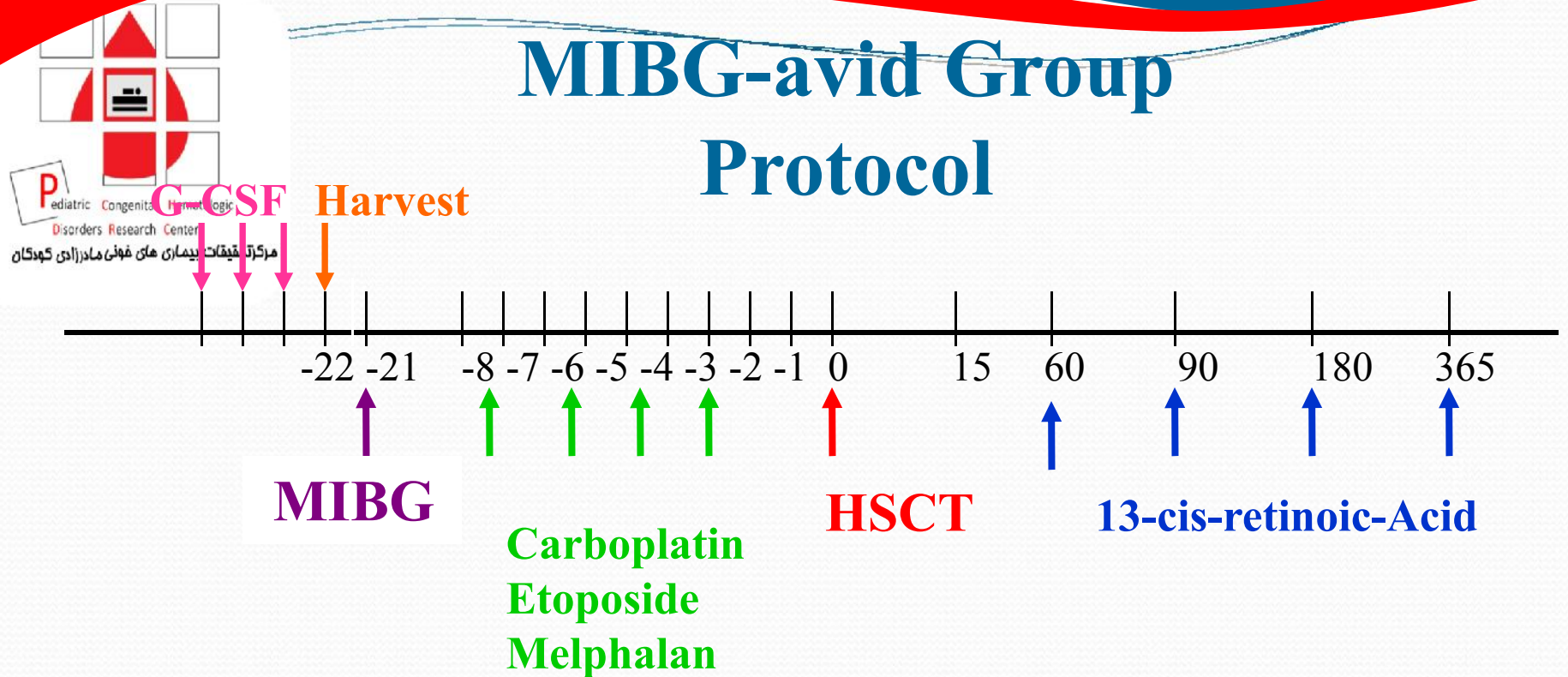
# Methods

- The conditioning regimen used in all patients consisted of
  1. Etoposide
  2. Carboplatin
  3. Melphalan

# Methods

- **Patients received 13-cis-retinoic-Acid 120-160 mg/m<sup>2</sup>/2 weeks per month, as maintenance from day sixty after HSCT until one year later.**

# MIBG-avid Group Protocol



**MIBG-avid patients received  $^{131}\text{I}$ -MIBG (12mci/kg) on day 21 before transplantation.**



# Non-MIBG-avid versus MIBG-avid ?



**MIBG-avid**

**BMT**

**non MIBG-avid**



# Results

- **Engraftment occurred in all patients.**
- **No severe side effects were observed in any patients in MIBG-avid group.**

# Results

- Patient age at diagnosis and transplant, diagnosis to transplant interval did not significantly associate with the outcome.
- Moreover patient sex, Shimada classification, N- MYC amplification and Pre-MIBG scan scores did not predict survival of patients.

# Results

- **The median time to neutrophil engraftment after ASCT was 10 days (range, 9-13 days) in MIBG avid and 11 days (range, 9-13 days) in MIBG non-avid subgroups.**
- **The median time to platelet engraftment was 13 days (range, 10-20 days) in MIBG avid cases and 12 days (range, 9-13 days) in MIBG-non-avid patients.**

# Results

- In MIBG avid patients, 3-y-OS was  $66\% \pm 21\%$  while in MIBG non-avid subgroup, 3-y-OS was  $53\% \pm 20\%$ .
- In MIBG avid and MIBG non-avid subgroups 3-y-EFS were  $66\% \pm 21\%$  and  $47\% \pm 19\%$  respectively.

# Conclusion

- **MIBG-avid patients showed better survival and lower relapse rate.**
- **It is, however, necessary to study large numbers of patients to determine the role of MIBG therapy in pre-transplant conditioning regimen for these patients.**

# Conclusion

- **These findings may suggest a more effective role for pre-transplant MIBG scintigraphy in high-risk neuroblastoma. Patients with MIBG avid lesions in pre-transplant scintigraphy may benefit from combination of therapeutic MIBG and higher dose of chemotherapy.**



# Conclusions

At this time a number of world's most advanced and complicated procedures of transplantation are being held in this section, including

- Unrelated transplantation
- Target therapy in pre-transplant conditioning regimen
- Transplant of one or two units of unrelated cord blood,
- Transplantation from Mesenchymal stem cells,
- Other relative transplantation
- Haploidentical transplantation
- Transplantation from mismatch related donors





# Pediatric SCT Unit

- S.Basirpanah
- A.Hosseini
- S.Bahrami
- V.Oskoie
- M.Masoudnia
- E.Nikoonesbati
- S.Mousavian
- F.Fakhraie
- E.Dolatkah
- L.Solaimani
- M.Safari
- L.Mosafer
- K.Boolori
- A.Yousefnejad
- P.Khosravi
- S.Nouroozi
- R.Asadian





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**10<sup>th</sup> AOCNMB**  
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◆◆◆ *Dr. Dabiri Award* ◆◆◆

*Amir Ali Hamidieh*

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IN NUCLEAR MEDICINE**

"Autologous hematopoietic stem cell transplantation in patients with high risk neuroblastoma treated with/without <sup>131</sup>I-MIBG"

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