

# Kök Hücre Nakli

veya bilinen adıyla

# Kemik İliđi Transplantasyonu

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Akdeniz Üniversitesi Tıp Fakültesi  
Çocuk Hematoloji Onkoloji BD

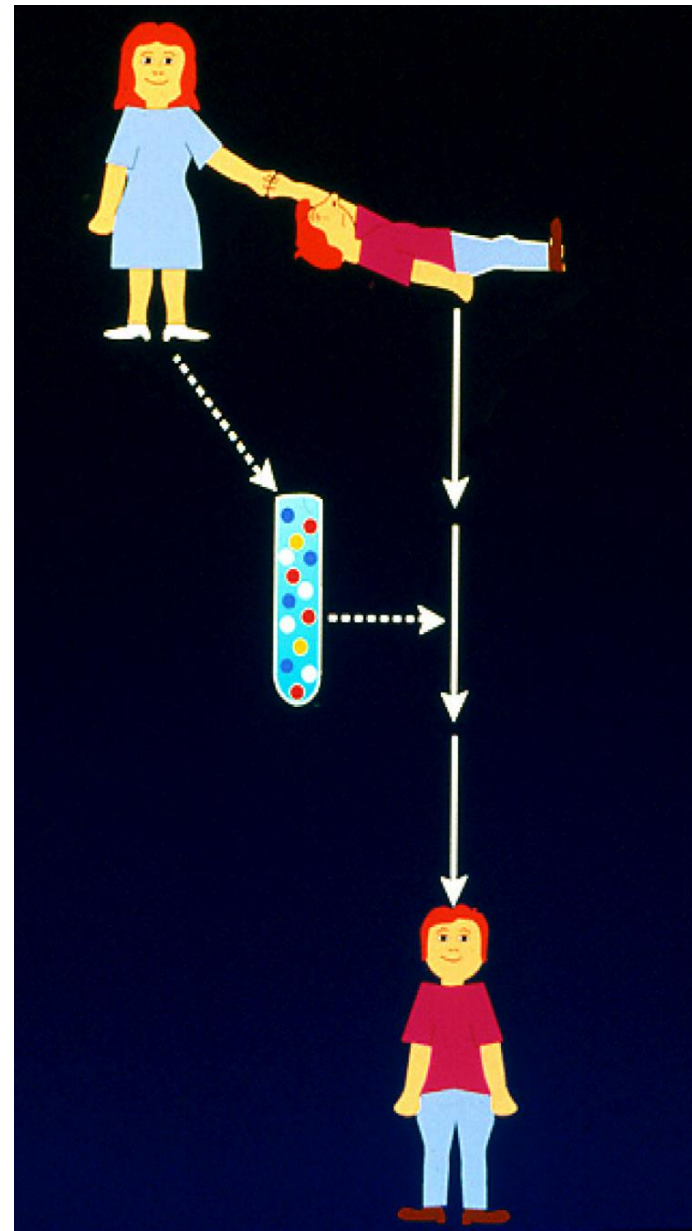
- Hemoglobinopatiler en sık görülen tek gen bozukluklarıdır.
- Dünya çapında milyonlarca insanı etkilediği tahmin ediliyor ve birçok ülke için önemli bir sağlık sorunu oluşturmaktadır.
- Düzenli transfüzyona ek olarak oral şelasyondaki gelişmeler ve destekleyici tedaviler yaşam beklentisini artırdı
- Hastaların yaşam kalitesini önemli hedef
- Tek küratif tedavi hematopoietik kök hücre naklidir

# Kaç Tipi Var?

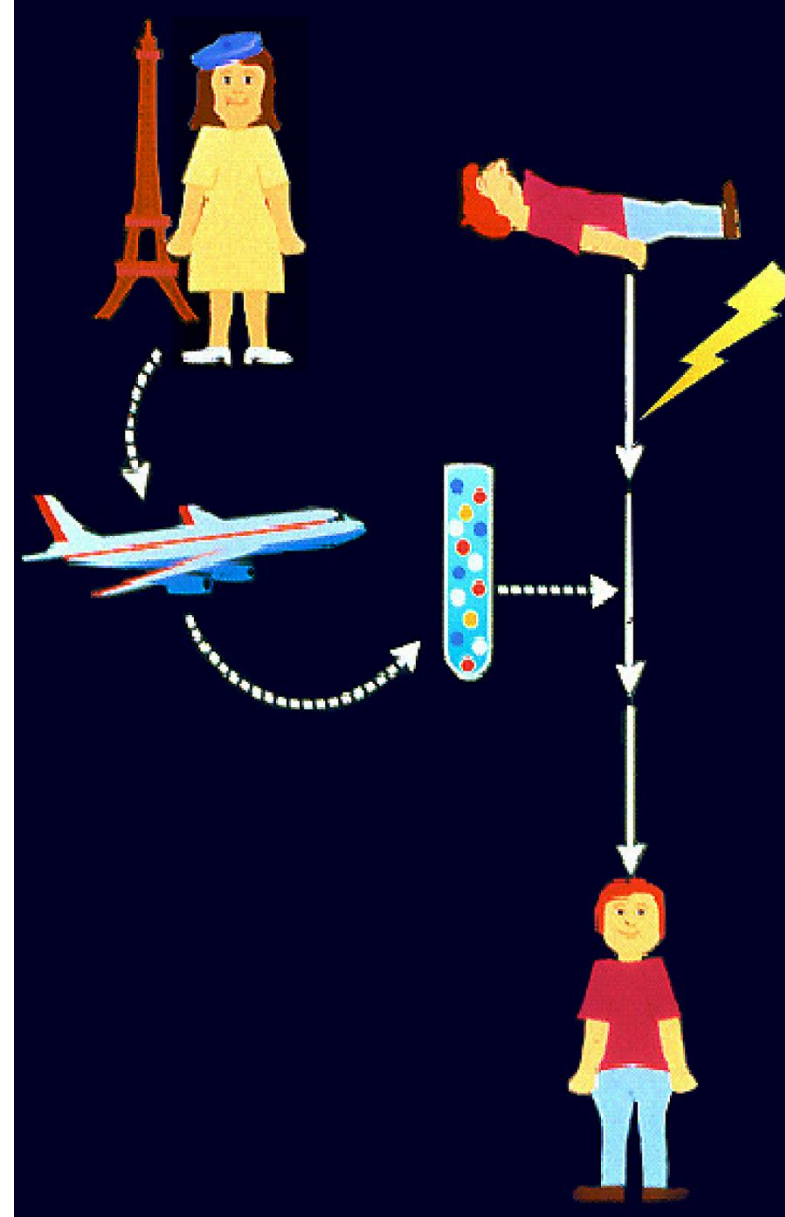
- Otolog
- Allojeneik
- Singeneik
  
- Kemik iliđi kaynaklı
- Periferik kök hücre kaynaklı
- Kordon kanı kaynaklı

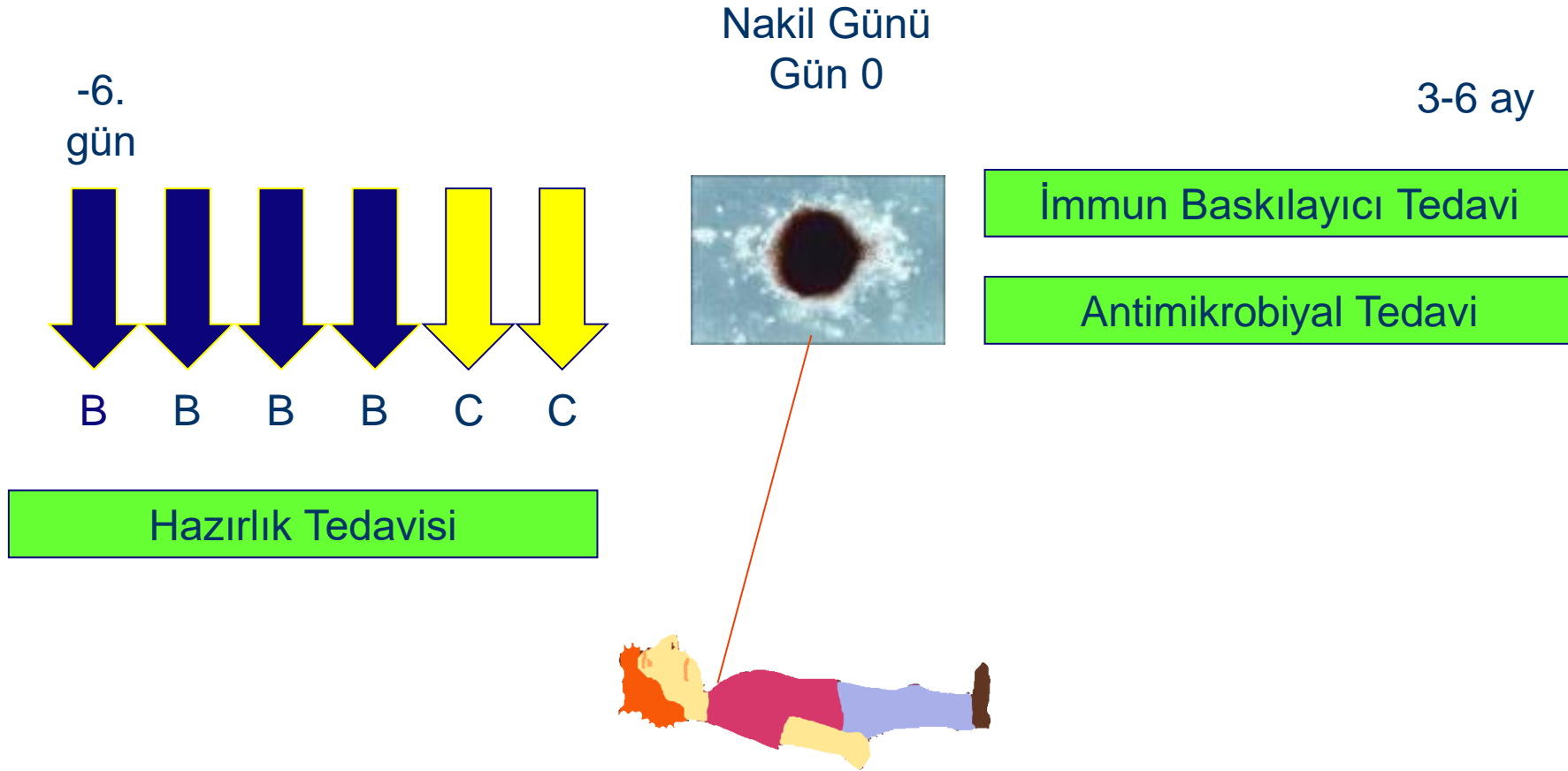
**Hematopoetik Hücre Nakli;**

**Allojenik**



## Akraba Dışı Verici Transplantasyonu





# Engrafmanı Sağlamak ve GVHH'yi Önlemek İçin Bağışıklığın Baskılanması



Büyüme Faktörü  
(BF)

Cyclosporine  
Methotrexate

Siprofloksasin  
(antibakteriyel)

Acyclovir (antiviral)

Fluconazole (antifungal)

Trimethoprim-  
sulfamethoxazole (Pneumocystis)



IV immunoglobulin



5,10 veya  
20 ml  
aspiratlar



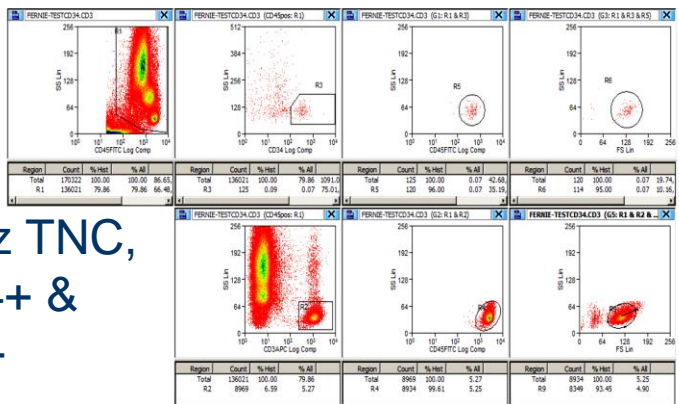
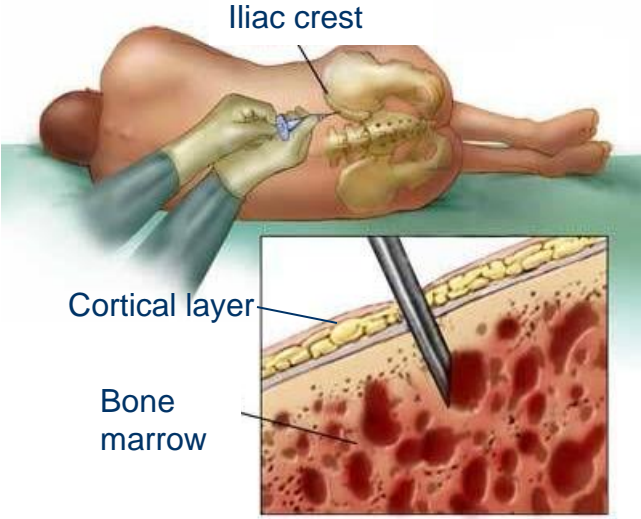
Alinan harvest  
torbasına



1 to 1.5ml  
örnekler

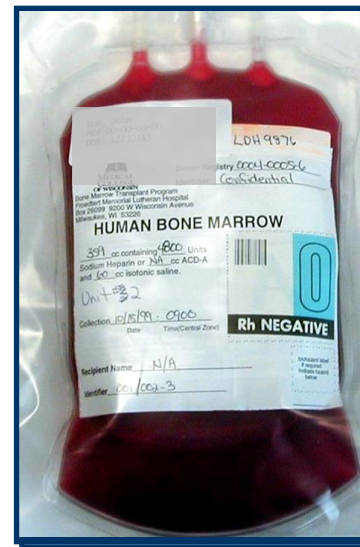


Lab işlemi



Analiz TNC,  
CD34+ &  
CD3+

# METOD





## ARTICLE



# Thalassemia-free and graft-versus-host-free survival: outcomes of hematopoietic stem cell transplantation for thalassemia major, Turkish experience

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We report the national data on the outcomes of hematopoietic stem cell transplantation (HSCT) for thalassemia major (TM) patients in Turkey on behalf of the Turkish Pediatric Stem Cell Transplantation Group. We retrospectively enrolled 1469 patients with TM who underwent their first HSCT between 1988 and 2020 in 25 pediatric centers in Turkey. The median follow-up duration and transplant ages were 62 months and 7 years, respectively; 113 patients had chronic graft versus host disease (cGVHD) and the cGVHD rate was 8.3% in surviving patients. Upon the last visit, 30 patients still had cGVHD (2.2%). The 5-year overall survival (OS), thalassemia-free survival (TFS) and thalassemia-GVHD-free survival (TGFS) rates were 92.3%, 82.1%, and 80.8%, respectively. cGVHD incidence was significantly lower in the mixed chimerism (MC) group compared to the complete chimerism (CC) group ( $p < 0.001$ ). In survival analysis, OS, TFS, and TGFS rates were significantly higher for transplants after 2010. TFS and TGFS rates were better for patients under 7 years and at centers that had performed over 100 thalassemia transplants. Transplants from matched unrelated donors had significantly higher TFS rates. We recommend HSCT before 7 years old in thalassemia patients who have a matched donor for improved outcomes.

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# Thalassemia-free and graft-versus-host-free survival: outcomes of hematopoietic stem cell transplantation for thalassemia major, Turkish experience

- 25 transplantasyon merkezi
- 32 yıllık deneyim (1988-2020)
- 1469 talasemi hastası
- 62 ay ortanca izlem süresi
- Ortanca yaş 7

Patient and transplant characteristics.

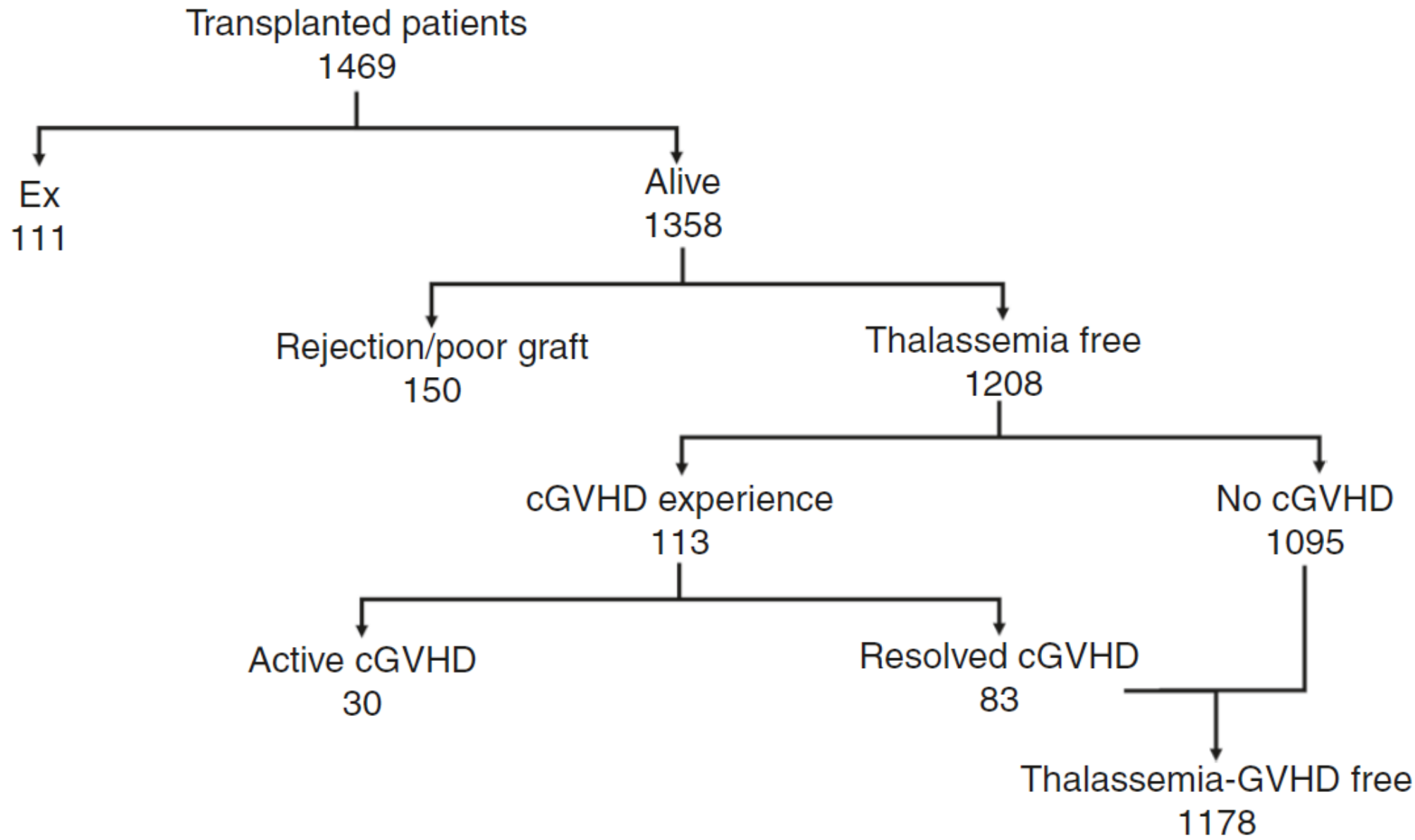
|                                    |                           |
|------------------------------------|---------------------------|
| <i>n</i>                           | 1469                      |
| Male/Female                        | 779/690                   |
| Median age                         | 7 years (1–29 years)      |
| Median follow-up                   | 62 months (15–402 months) |
| Transplant period                  |                           |
| Before 2010                        | 254                       |
| After 2010                         | 1215                      |
| Center experience                  |                           |
| <100 Thalassemia transplant        | 578                       |
| >100 Thalassemia Transplant        | 891                       |
| Stem Cell Source                   |                           |
| Bone Marrow                        | 953                       |
| Peripheral Blood                   | 380                       |
| Bone Marrow+Cord Blood             | 118                       |
| Unknown                            | 18                        |
| Donor type                         |                           |
| Matched Sibling                    | 1020                      |
| Matched Related                    | 194                       |
| Matched Unrelated                  | 255                       |
| Unrelated Donor Matching           |                           |
| 9/10                               | 44                        |
| 10/10                              | 211                       |
| cGVHD experience in alive patients |                           |
| Yes                                | 113                       |
| No                                 | 1245                      |

*cGVHD* chronic graft versus host disease.

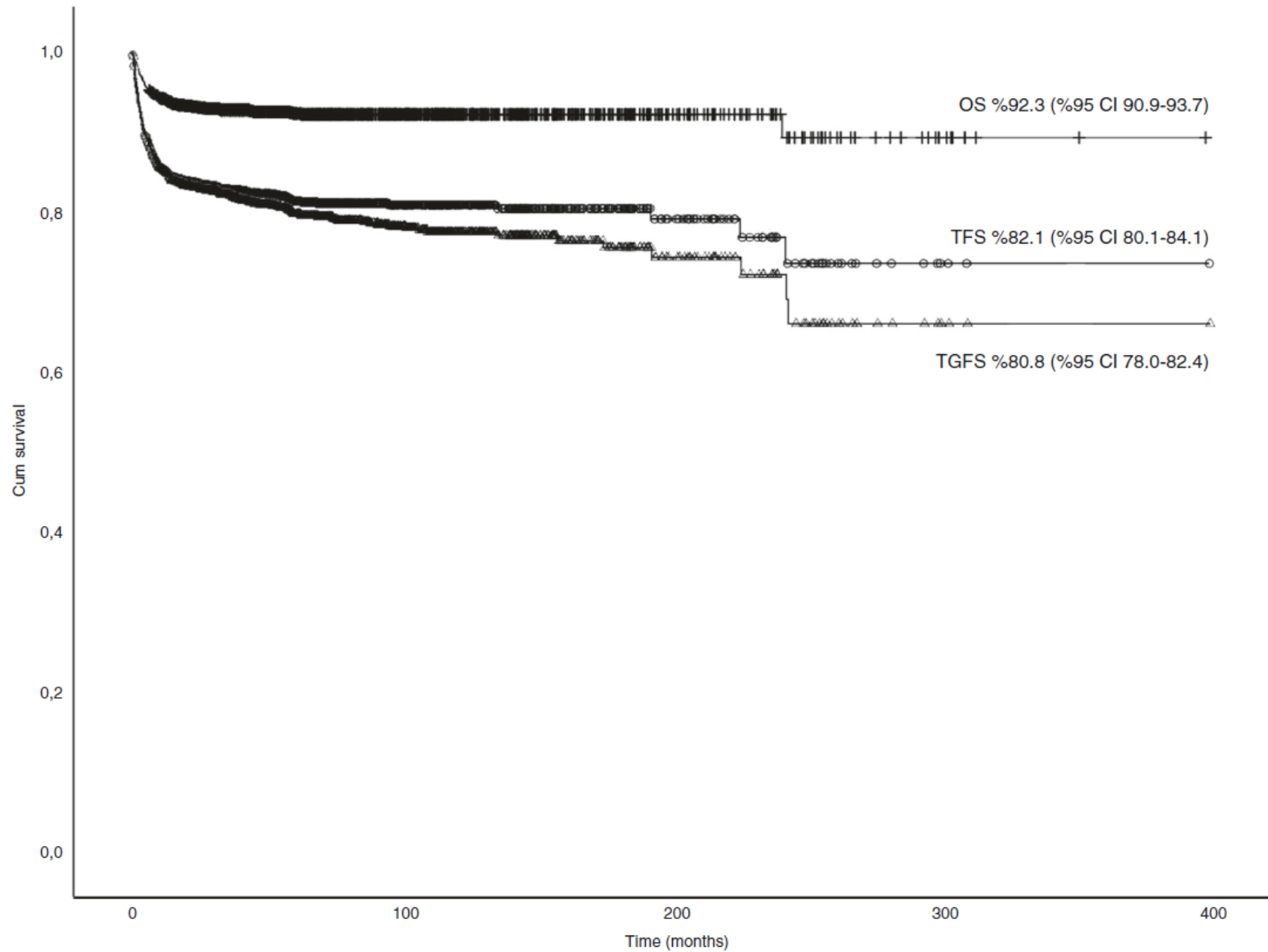
**Table 2.** Univariate analysis of prognostic factors after 1st HSCT in thalassemia major patients for 5 years survival analysis.

|                                       | <i>n</i> | <i>OS</i>                | <i>p</i> | <i>TFS</i>                | <i>p</i> | <i>TGFS</i>              | <i>p</i> |
|---------------------------------------|----------|--------------------------|----------|---------------------------|----------|--------------------------|----------|
| All patients                          | 1469     | 92.3% (95% CI 90.9–93.7) |          | 82.1% (95% CI 80.1–84.1)  |          | 80.8% (95% CI 78.0–82.4) |          |
| <i>Donor chimerism</i>                |          |                          |          |                           |          |                          |          |
| Full chimeric                         | 1055     | 94.7% (95% CI 93.3–96.1) | 0.65     | 94.6% (95% CI 93.2–96.0)  | 0.88     | 92.9% (95% CI 91.3–94.5) | 0.16     |
| Mixed chimeric                        | 194      | 95.3% (95% CI 92.3–98.4) |          | 95.3% (95% CI 92.3–98.4)  |          | 95.3% (95% CI 92.3–98.4) |          |
| <i>Transplant age</i>                 |          |                          |          |                           |          |                          |          |
| <7 years old                          | 762      | 93.7% (95% CI 91.9–95.5) | 0.06     | 84.3% (95% CI 81.5–87.1)  | 0.02     | 83.3% (95% CI 80.5–86.1) | 0.01     |
| >7 years old                          | 707      | 90.7% (95% CI 88.5–92.9) |          | 79.8% (95% CI 76.8–82.8)  |          | 78.0% (95% CI 74.8–81.2) |          |
| <i>Gender</i>                         |          |                          |          |                           |          |                          |          |
| Male                                  | 779      | 91.8% (95% CI 89.8–93.8) | 0.49     | 80.8% (95% CI 78.0–83.6)  | 0.16     | 79.8% (95% CI 76.8–82.8) | 0.49     |
| Female                                | 690      | 92.8% (95% CI 90.8–94.8) |          | 83.7% (95% CI 80.9–86.5)  |          | 81.9% (95% CI 78.9–84.9) |          |
| <i>Donor type</i>                     |          |                          |          |                           |          |                          |          |
| MSD                                   | 1020     | 92.7% (95% CI 91.1–94.3) | 0.04     | 82.1% (95% CI 79.7–84.5)  | <0.01    | 81.7% (95% CI 79.3–84.1) | <0.01    |
| MRD                                   | 194      | 88.0% (95% CI 83.2–92.8) |          | 74.9% (95% CI 68.5–81.3)  |          | 72.9% (95% CI 66.3–79.5) |          |
| MUD                                   | 255      | 94.1% (95% CI 91.1–97.1) |          | 88.6% (95% CI 84.6–92.6)  |          | 82.6% (95% CI 77.2–88.0) |          |
| <i>MUD Donor</i>                      |          |                          |          |                           |          |                          |          |
| 9/10                                  | 44       | 88.4% (95% CI 79.0–98.6) | 0.09     | 74.9% (95% CI 61.7–88.1)  | <0.01    | 66.5% (95% CI 50.3–82.7) | <0.01    |
| 10/10                                 | 210      | 95.2% (95% CI 92.2–98.2) |          | 91.4% (95% CI 87.6–95.2)  |          | 85.8% (95% CI 80.4–91.2) |          |
| <i>Transplant period</i>              |          |                          |          |                           |          |                          |          |
| <2010                                 | 254      | 87.1% (95% CI 82.9–91.3) | <0.01    | 71.3 % (95% CI 65.7–76.9) | <0.01    | 71.3% (95% CI 65.7–76.9) | <0.01    |
| >2010                                 | 1215     | 93.4% (95% CI 92.0–94.8) |          | 84.5 % (95% CI 82.3–86.7) |          | 82.8% (95% CI 80.6–85.0) |          |
| <i>Center experience</i>              |          |                          |          |                           |          |                          |          |
| <100 TM transplant                    | 578      | 91.1% (95% CI 88.5–93.7) | 0.22     | 78.4% (95% CI 74.8–82.0)  | <0.01    | 77.4% (95% CI 73.8–81.0) | <0.01    |
| >100 TM transplant                    | 891      | 93.0% (95% CI 91.2–94.8) |          | 84.5% (95% CI 82.1–86.9)  |          | 82.9% (95% CI 80.3–85.5) |          |
| <i>cGVHD</i>                          |          |                          |          |                           |          |                          |          |
| No                                    | 1339     | 92.9% (95% CI 91.5–94.3) | 0.02     | 81.8% (95% CI 79.6–84.0)  | 0.14     |                          |          |
| Yes                                   | 130      | 86.8% (95% CI 80.2–93.0) |          | 84.8% (95% CI 78.0–91.6)  |          |                          |          |
| <i>Stem Cell Source Sibling Donor</i> |          |                          |          |                           |          |                          |          |
| BM                                    | 717      | 93.9% (95% CI 92.1–95.7) | <0.01    | 82.8% (95% CI 80.0–85.6)  | 0.02     | 82.4% (95% CI 79.4–85.4) | 0.02     |
| PB                                    | 169      | 85.6% (95% CI 80.2–91.0) |          | 73.3% (95% CI 66.5–80.1)  |          | 72.6% (95% CI 65.8–79.4) |          |
| <i>MUD Donor</i>                      |          |                          |          |                           |          |                          |          |
| BM                                    | 124      | 91.9% (95% CI 86.9–96.9) | 0.17     | 83.7% (95% CI 77.1–90.3)  | 0.02     | 81.5% (95% CI 74.3–88.7) | 0.33     |
| PB                                    | 131      | 96.1% (95% CI 92.7–99.5) |          | 93.1% (95% CI 88.7–97.5)  |          | 82.5% (95% CI 74.1–90.9) |          |
| <i>All Patients</i>                   |          |                          |          |                           |          |                          |          |
| BM                                    | 953      | 93.1% (95% CI 91.5–94.7) | 0.02     | 81.7% (95% CI 78.9–84.3)  | 0.12     | 80.9% (95% CI 78.3–83.5) | 0.03     |
| BM + CB                               | 118      | 95.8% (95% CI 92.0–99.6) |          | 89.0% (95% CI 84.2–94.8)  |          | 89.0% (95% CI 83.2–94.8) |          |
| PB                                    | 380      | 89.1% (95% CI 85.9–92.2) |          | 80.5% (95% CI 76.3–84.7)  |          | 77.1% (95% CI 72.5–81.7) |          |

*OS* overall survival, *TFS* thalassemia-free survival, *TGFS* thalassemia-GVHD free survival, *MSD* matched sibling donor, *MRD* matched related donor, *MUD* matched unrelated donor, *TM* thalassemia major, *BM* bone marrow, *CB* cord blood, *PB* peripheral blood.







**Fig. 2** The 5-year probabilities of overall, thalassemia-free and thalassemia-GVHD-free survival for thalassemia major patients.

Multivariate analysis of the prognostic factors.

|                          | OS            | TFS   |               | TGFS  |               |       |
|--------------------------|---------------|-------|---------------|-------|---------------|-------|
|                          | HR (%95 CI)   | p     | HR (%95 CI)   | p     | HR (%95 CI)   | p     |
| <i>Transplant age</i>    |               |       |               |       |               |       |
| → <7 years old           | 1             |       | 1             |       | 1             |       |
| >7 years old             | 1.5 (1.0–2.2) | 0.03  | 1.4 (1.1–1.7) | <0.01 | 1.4 (1.1–1.8) | <0.01 |
| <i>cGVHD</i>             |               |       |               |       |               |       |
| No                       | 1             |       | 1             |       | 1             |       |
| Yes                      | 1.6 (0.9–2.7) | 0.10  | 0.6 (0.4–1.0) | 0.07  | -             |       |
| <i>Donor type</i>        |               |       |               |       |               |       |
| → MSD                    | 1             |       | 1             |       | 1             |       |
| MRD                      | 1.5 (0.9–2.6) | 0.07  | 1.6 (1.1–2.2) | <0.01 | 1.6 (1.2–2.2) | <0.01 |
| MUD                      | 0.9 (0.5–1.7) | 0.79  | 0.8 (0.5–1.3) | 0.38  | 1.0 (0.7–1.5) | 0.96  |
| <i>Stem Cell Source</i>  |               |       |               |       |               |       |
| → BM                     | 1             |       | 1             |       | 1             |       |
| BM + CB                  | 0.6 (0.2–1.5) | 0.30  | 0.5 (0.3–0.9) | 0.04  | 0.5 (0.3–0.9) | 0.03  |
| PB                       | 1.3 (0.8–2.0) | 0.28  | 0.9 (0.7–1.2) | 0.53  | 0.9 (0.7–1.2) | 0.62  |
| <i>Transplant period</i> |               |       |               |       |               |       |
| → Before 2010            | 1             |       | 1             |       | 1             |       |
| After 2010               | 0.5 (0.3–0.8) | <0.01 | 0.5 (0.4–0.7) | <0.01 | 0.6 (0.4–0.8) | <0.01 |
| <i>Center experience</i> |               |       |               |       |               |       |
| → <100 TM transplant     | 1             |       | 1             |       | 1             |       |
| >100 TM transplant       | 0.7 (0.5–1.0) | 0.10  | 0.7 (0.5–0.9) | <0.01 | 0.7 (0.6–0.9) | <0.01 |

OS overall survival, TFS thalassemia-free survival, TGFS thalassemia-GVHD free survival, MSD matched sibling donor, MRD matched related donor, MUD matched unrelated donor, BM bone marrow, CB cord blood, PB peripheral blood, TM thalassemia major.

Some recent publications which report the outcomes after HSCT in patients with thalassemia.

| Author          | Country                    | Publishing Year | Transplant interval | n    | Donor type           | Follow-up Median | OS %   | TFS %          | TGFS % | Comment   |
|-----------------|----------------------------|-----------------|---------------------|------|----------------------|------------------|--|----------------|--------|---|
| Alonso [33]     | Spain                      | 2019            | 1989–2014           | 43   | MSD, MRD, MUD        | 3 years          | 92   | 81             | NA     | In 6 centers in Spain   |
| Choudhary [32]  | India                      | 2019            | 2008–2017           | 203  | MSD, MRD, MUD, Haplo | 29 months        | 88.5   | 82             | NA     | 12.9% cGVHD   |
| Li [21]         | China, India, USA          | 2019            | 2000–2016           | 1110 | MSD, MRD, MUD, Haplo | 5 years          | ≤6 years old 90<br>7–15 years old 84<br>16–25 years old 63 | 86<br>80<br>63 | NA     | An International study, 90% of patients in the last decade                          |
| Galambrun [16]  | France                     | 2013            | 1985–2007           | 108  | MSD, MRD, MUD        | 12 years         | 86.8   | 69.4           | NA     | 96 siblings, 12 cGVHD   |
| Caocci [34]     | Italy                      | 2017            | 1987–2016           | 258  | MSD, MUD             | 11 years         | 82.6   | 77.8           | NA     | Adult OS 70, TFS 67.3, cGVHD 12.9%  |
| Ramprakash [12] | India, Pakistan, Sri Lanka | 2017            | 2013–2016           | 71   | MSD                  | 17.5 months      | 93   | 83             | 74.6   | BU oral, CY, ATG, cGVHD 4%  |
| Li [13]         | China                      | 2019            | 2007–2018           | 184  | MSD                  | 3 years          | 97.8   | 97.3           | 89.5   | G-CSF-Mobilized Blood and BM Grafts   |
| Lai [14]        | China                      | 2021            | 2007–2019           | 521  | MSD, MUD, Haplo      | 3 years          | 94.3   | 92.5           | 86.9   | VOD 10.4%   |
| Current study   | Turkey                     | 2021            | 1988–2020           | 1469 | MSD, MRD, MUD        | 62 months        | 92.3   | 82.1           | 80.8   | Only first transplantation results, whole country results from 25 pediatric centers |

OS overall survival, TFS thalassemia-free survival, TGFS thalassemia-GVHD free survival, MSD matched sibling donor, MRD matched related donor, MUD matched unrelated donor, BM bone marrow, PB peripheral blood, cGVHD chronic Graft Versus Host Disease, BU busulphan, CY cyclophosphamide, VOD veno-occlusive disease.



- Nakil 7 yařından önce yapılmalı
- Tam uyumlu MUD ile MSD başarısı karşılaştırılabilir
- GvHH olmadan yaşam kalitesini korumak önemli
- Kronik GvHH: %8.3
- Genel sağkalım %92.3
- Talasemisiz sağkalım %82.1
- Talasemisiz GvHHsiz sağkalım %80.8

**Teşekkür ederim**