Myelofibrosis and transplantation French version

French & British day on behalf the

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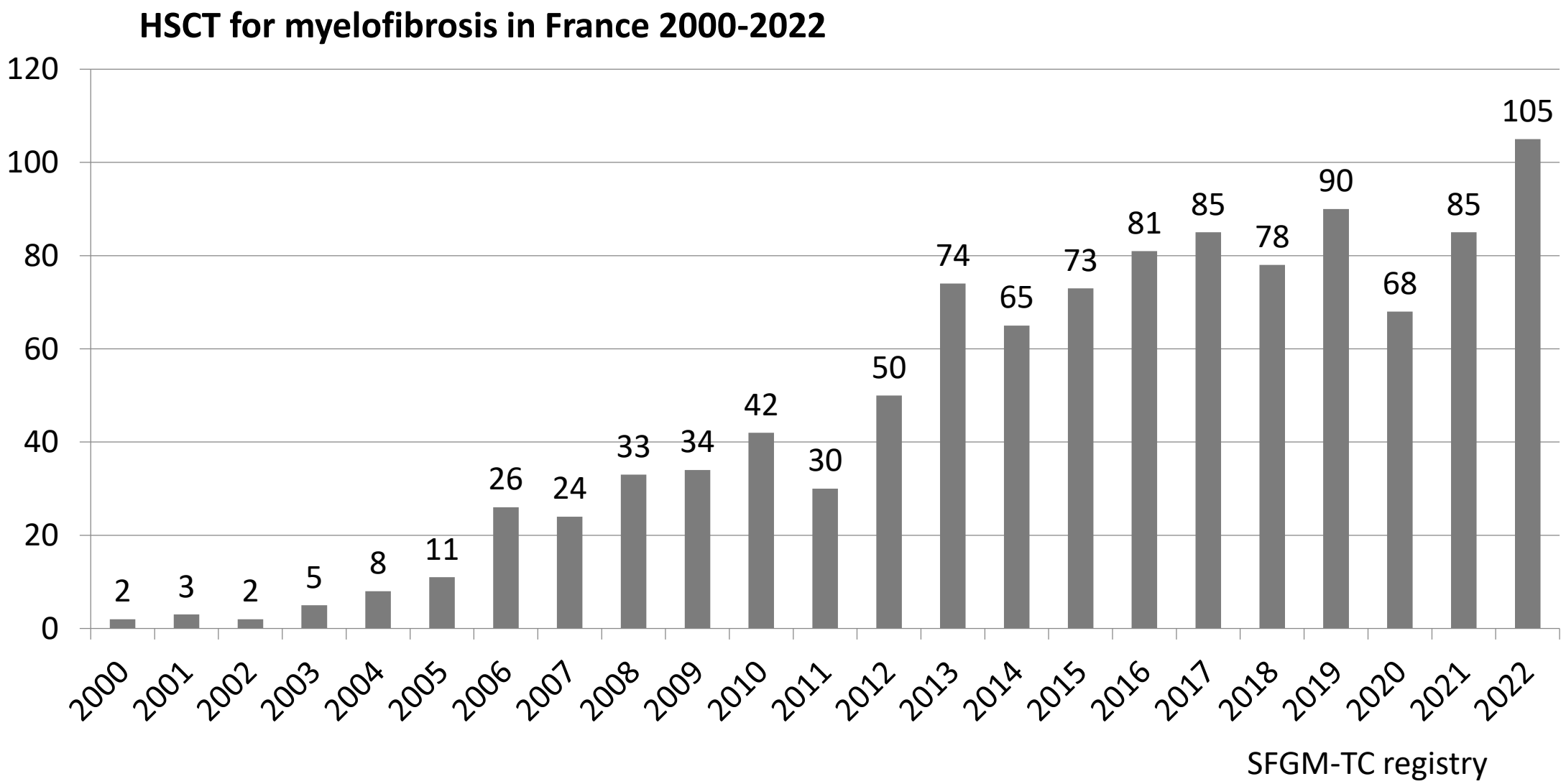
Introduction

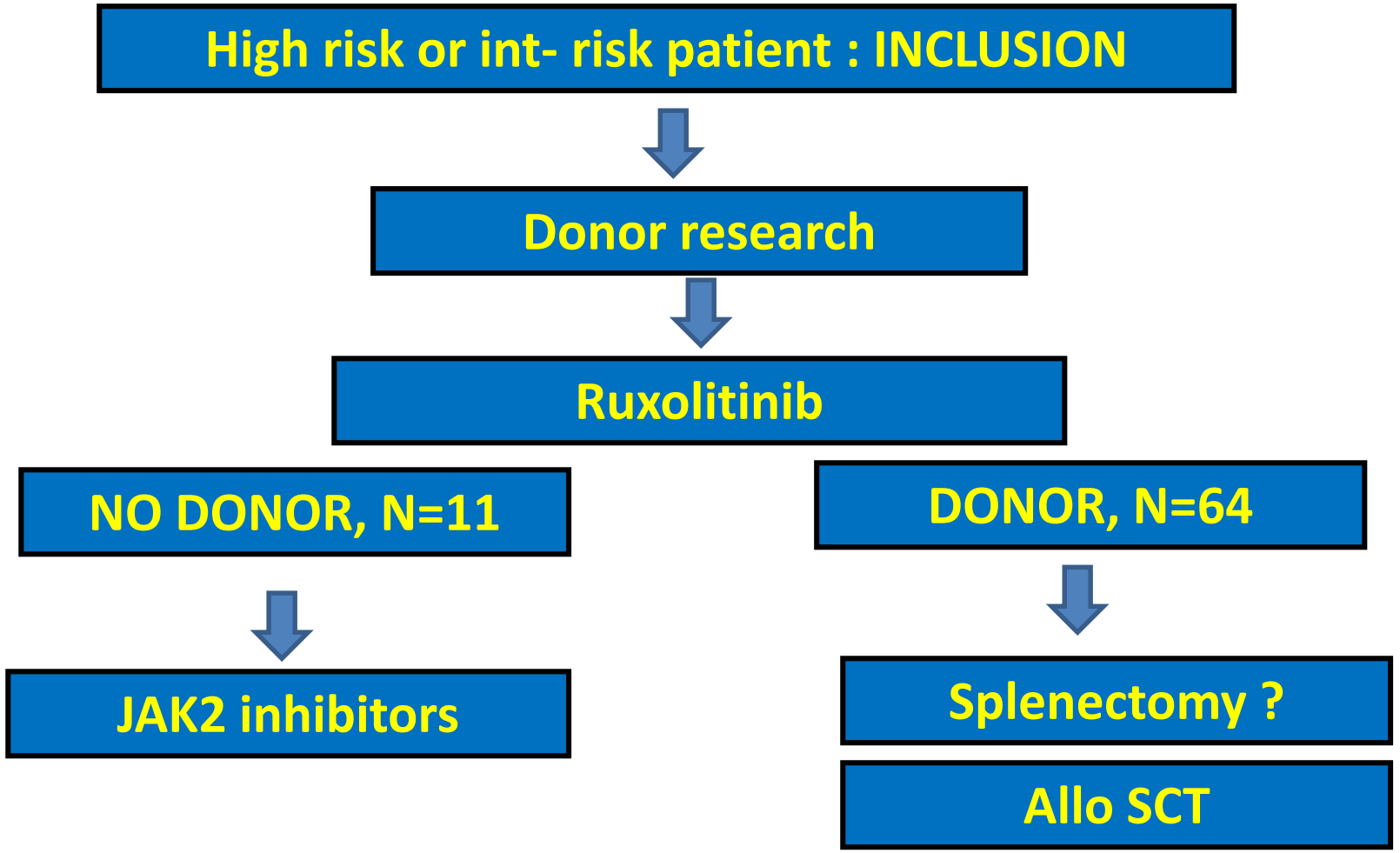


JAK ALLO STUDY

« JAK2 RUXOLITINIB before allogeneic hematopoietic stem cell transplantation in primary or secondary myelofibrosis: a prospective phase II trial »

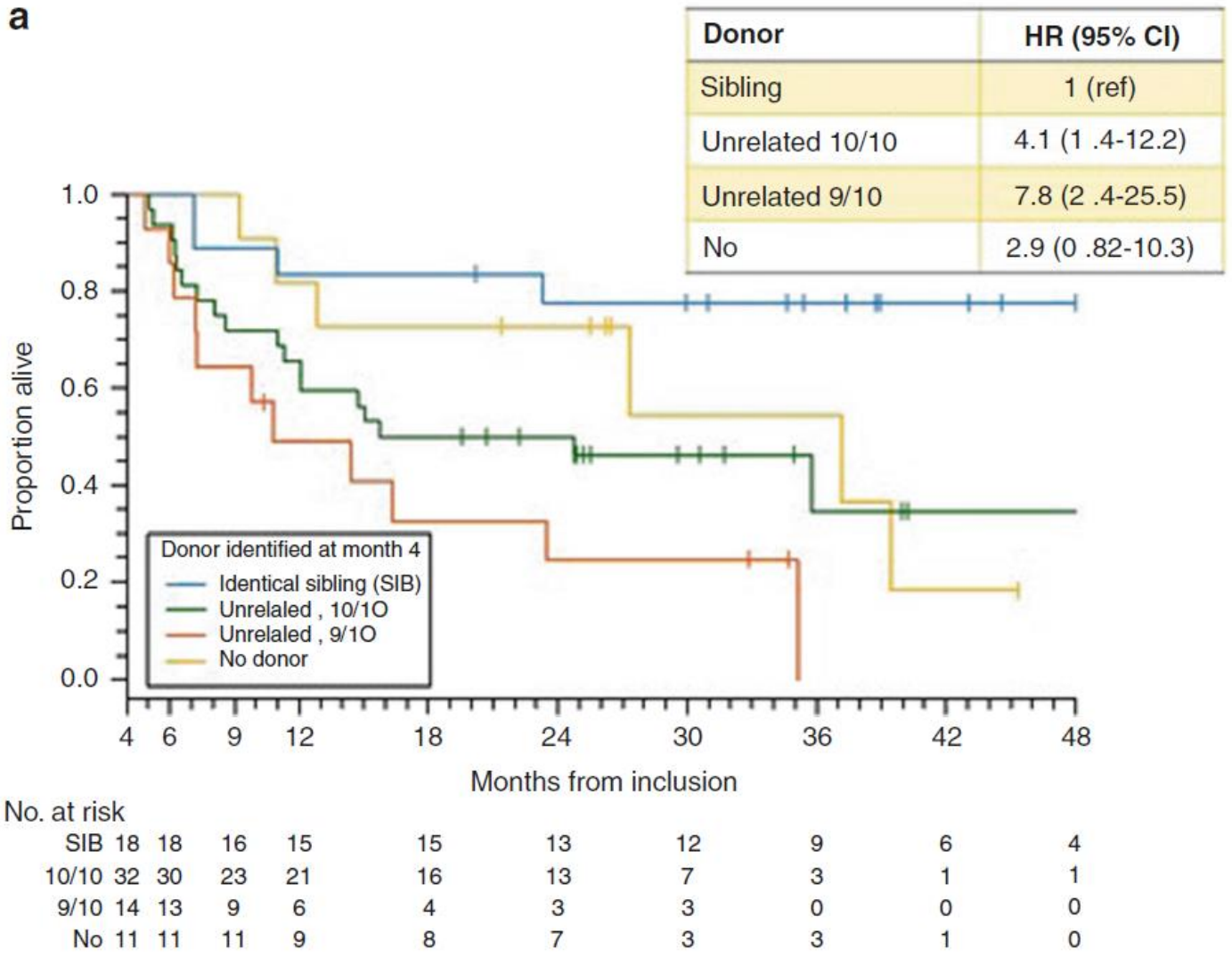
Primary objective was DFS at one year after 6-month course of ruxolitinib

DESIGN STUDY



Messages of the JAK ALLO

- 92% of patients with a transplanted after ruxolitinib
- Hyperacute GVHD (32%) & grade 3-4 (44%) acute GVHD was high
- Other SAE: RWS, heart failure (4 cardiogenic shocks), TLS
- Abrupt stopping of ruxo give better NRM than progressive discontinuation
- The main risk factor was the type of donor



Messages from registry, JAK ALLO & others

- Results with the use of an unrelated donor AND fludarabine-melphalan conditioning regimen are disappointing
- MF patients may have SIRS shortly after transplantation but the role of ruxo is not easy to determine
- Patients who are not responders to ruxo have worse outcome than responders (confirmed by Kroger et al, in Leukemia 2021, *non significant in MVA*) **=> should we delay transplant in patient under ruxo ?**
- New regimens are tested, especially in the setting of an unrelated donor (treosulfan?)
- PCTY is largely used in 9/10 donor
- Role of haplo?

Haplo-identical transplantation in myelofibrosis « FIBRAPLO »: A phase II trial

SFGM-TC & FIM

DRCI Hôpital Saint-Louis, APHP

Main objective

- The hypothesis is that survival without event (disease or rejection) is more than 55% one year after transplantation instead of 30%.

- A two-side, one-sample logrank test calculated from a sample of **28 subjects**, 90% power at a 0.050 significance level to detect a proportion of survival of 55% in the new group when the proportion surviving in the historic control is 25%. These proportions surviving are for a period of 1 year. Subjects are accrued for a period of 24 months. Follow-up continues for a period of 12 months after the last subject is added.

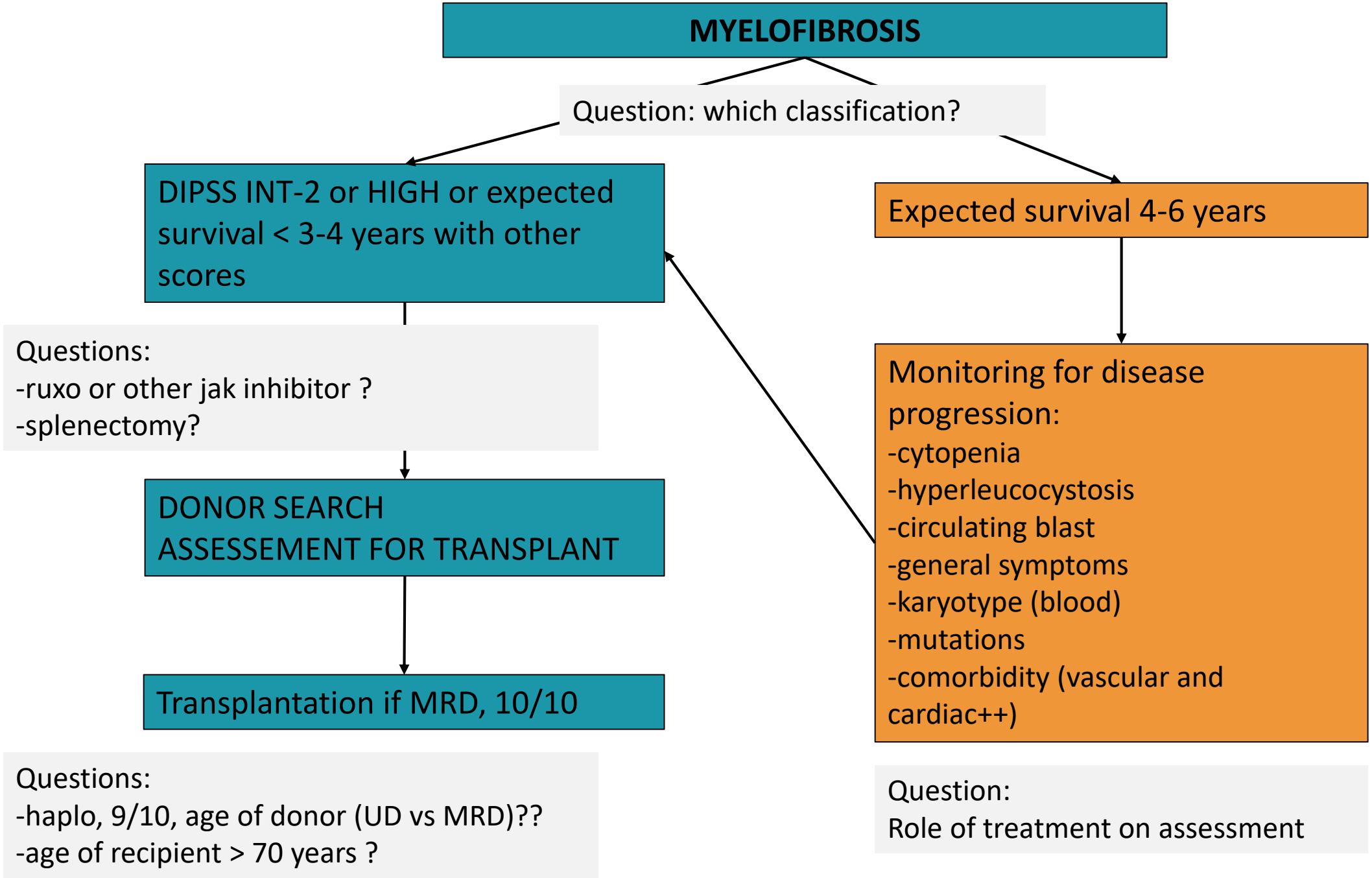
Inclusion criteria

- Primary myelofibrosis or myelofibrosis secondary to essential thrombocythemia or polycythemia Vera proven by marrow biopsy
- The myelofibrosis should combine at least 2 of the following criteria:
  - constitutional symptoms: weight loss > 10% in one year, fever (without infection), recurrent muscle, bone or join pains, extreme fatigue
  - anemia with hemoglobin < 10 gr/dL or red blood cell transfusion
  - thrombocytopenia < 100 G/L
  - peripheral blast count > 1% at least found 2 times
  - white blood cell count > 25 G/L (before a cytoreductive treatment)
  - Karyotype: +8, -7/7q-, i(17q), -5, 5q-, 12p-, inv(3), 11q23
  - wild type CALR and ASXL1 or TP53 mutation
- Patients younger than 70 years
- Performance status according to ECOG at 0, 1 or 2
- No HLA matched donor

Transplant regimen

- **Conditioning regimen**
  - Fludarabine 30 mg/m^2/day for 5 days on day-5, -4, -3, -2 and -1
  - Thiotepa 5mg/kg/day for one day on day-6
  - Treosulfan 10 gr/m2 body surface area /day for 3 days on day -4, -3 and -2

- **GVHD prophylaxis**
  - Cyclosporine from day -1
  - Mycophenolate mofetil from day +1
  - Cyclophosphamide on day 3 and 5


MYELOFIBROSIS
Question: which classification?
DIPSS INT-2 or HIGH or expected survival < 3-4 years with other scores
Expected survival 4-6 years
Questions:
-ruxo or other jak inhibitor ?
-splenectomy?
DONOR SEARCH
ASSESSEMENT FOR TRANSPLANT
Transplantation if MRD, 10/10
Monitoring for disease progression:
-cytopenia
-hyperleucocystosis
-circulating blast
-general symptoms
-karyotype (blood)
-mutations
-comorbidity (vascular and cardiac++)
Questions:
-haplo, 9/10, age of donor (UD vs MRD)??
-age of recipient > 70 years ?
Question:
Role of treatment on assessment