Eosinophil malignancies

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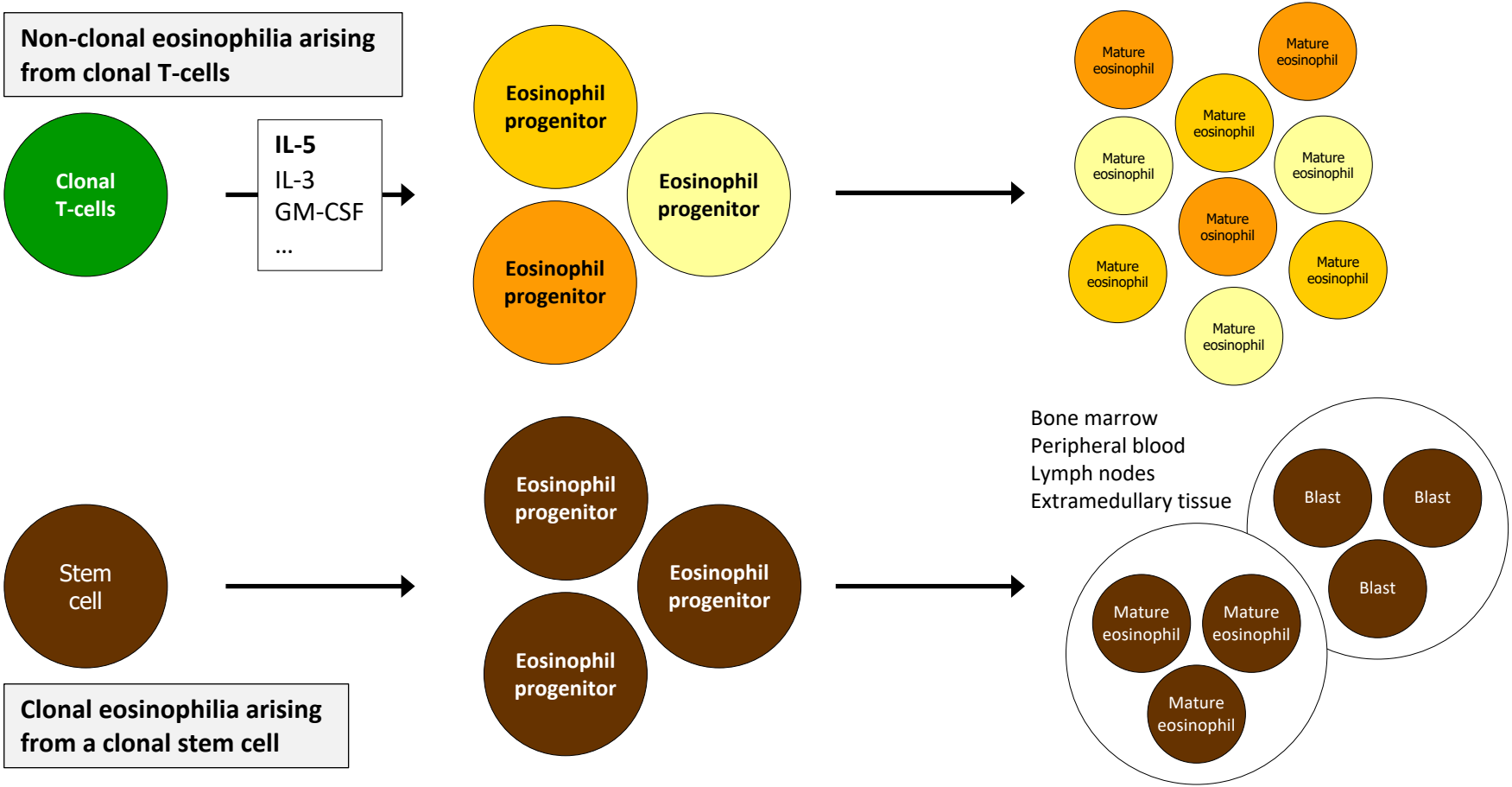
Disclosures

Name of Company	Research support (clinical trials)	Consultant/ Scientific Advisory Board	Honoraria	Travel reimbursement
Blueprint	x	x	x	x
Novartis	x	x	x	x
BMS	x	x	x	x
AOP	x	x	x	x
GSK	x	x	x	x
Abbvie	x	x	x	x
Incyte	x	x		
Cogent	x	x		
Astra Zeneca	x			

Non-clonal and clonal eosinophilia



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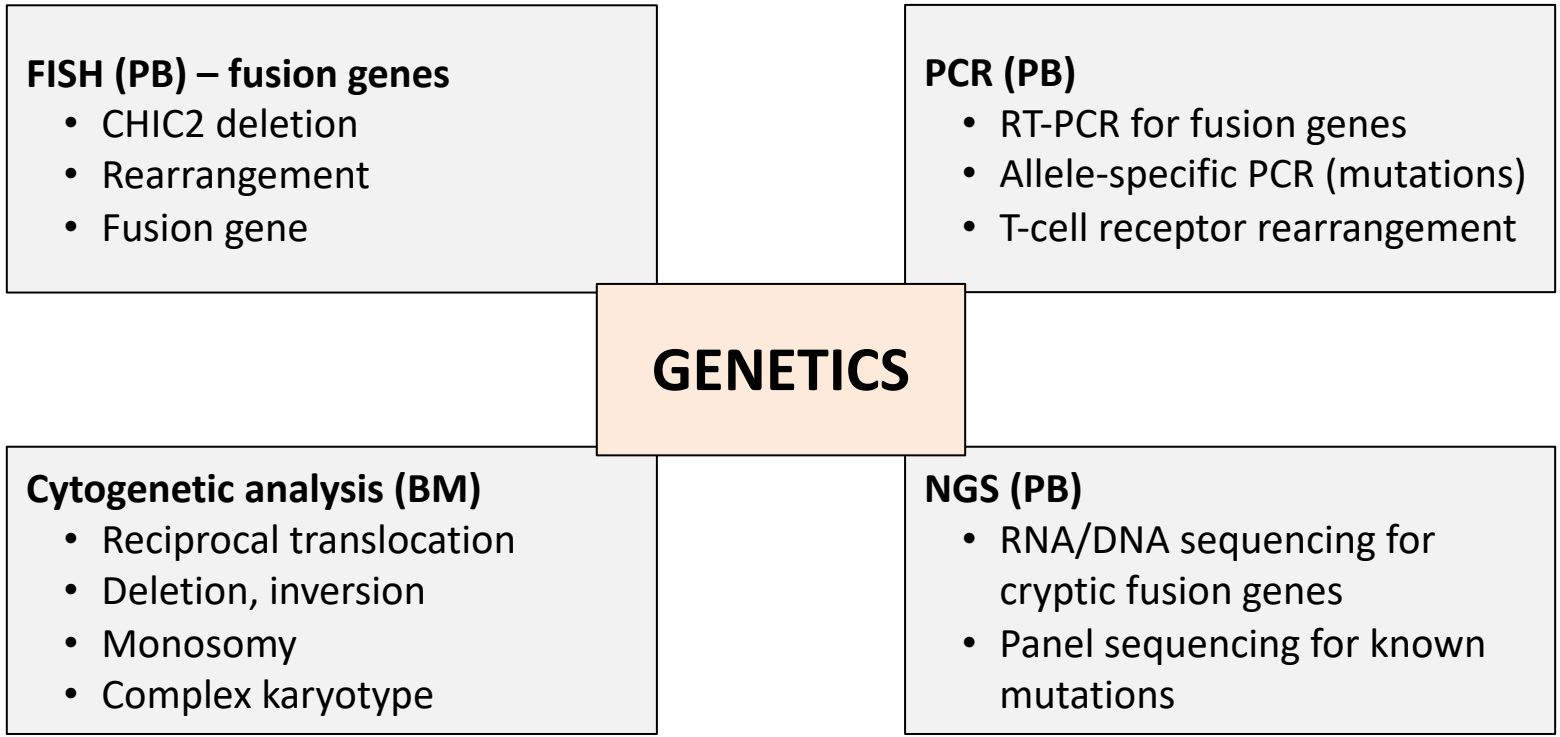
Basic genetic techniques in the diagnostic work-up of eosinophilia



BM: bone marrow; NGS: next generation sequencing; PB: peripheral blood

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Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase fusion genes (MLN-eo-TK)

Fusion	Partner genes	No. of patients n=135	Myeloid/lymphoid blast phase (BM or EMD) n=38 (28%)	Primary/ secondary blast phase (25/13)
FIP1L1::PDGFRA	1	78	**17 (22%)**	**13 / 4**
PDGFRB	11	26	**5 (19%)**	**4 / 1**
FGFR1	3	9	**7 (78%)**	**6 / 1**
JAK2	2	11	**3 (27%)**	**0 / 3**
ETV6::ABL1	1	11	**6 (54%)**	**2 / 4**

BM: bone marrow
EMD: extramedullary disease („lymphoma“; „myeloid sarcoma“)

German Registry for Disorders of Eosinophils and Mast Cells (GREM)
Metzgeroth et al., submitted

M/LN-eo with *PDGFRA/PDGFRB* fusions

***PDGFRA/PDGFRB* (n=104)**

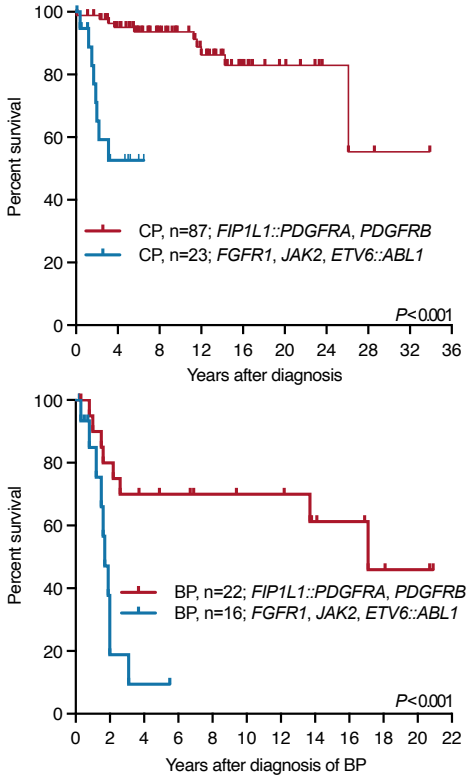
- *FIP1L1::PDGFRA* (n=78)
- *PDGFRB* (n=26; various fusion partners, n=11)

Chronic phase (n=87)

- Progression into secondary BP (n=5; *PDGFRA*, n=4, *PDGFRB*, n=1)
- Allogeneic SCT in CP (n=3)
- Causes of death (n=8)
  - Comorbidity (n=5)
  - **Resistance/progression (n=1)**
  - **Resistance/allogeneic SCT/GvHD (n=1)**
  - Cardiac involvement (n=1)

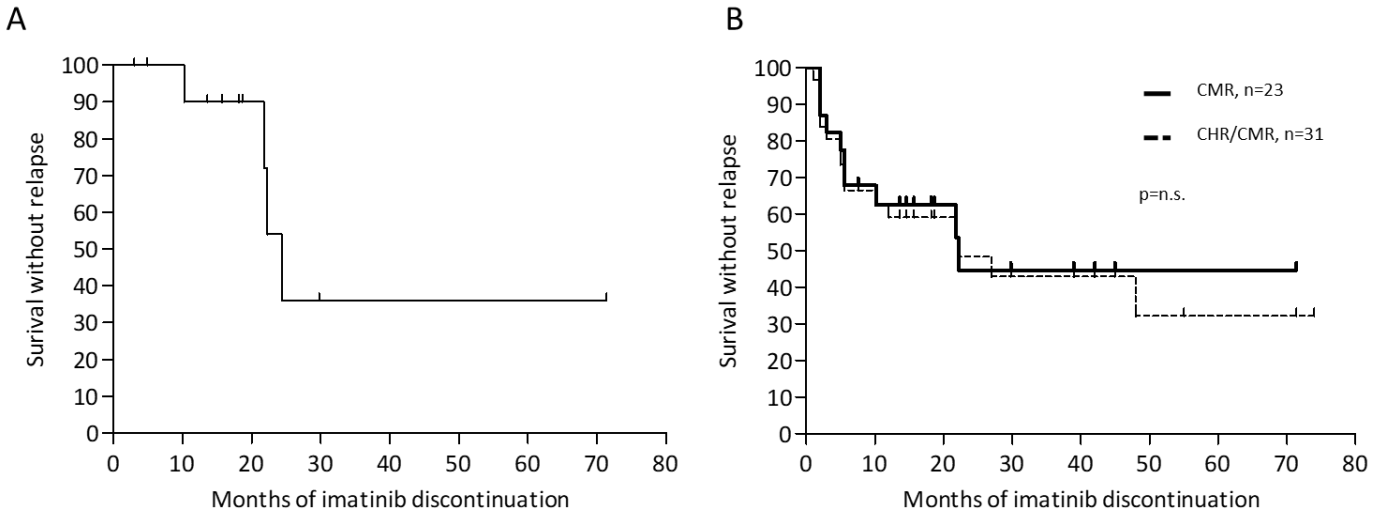
Blast phase (n=22)

- Primary (n=17), secondary (n=5)
- Allogeneic SCT (n=6)
- Causes of death (n=8; primary, n=6; secondary, n=2)
  - **Resistance/relapse (n=4)**
  - Comorbidity (n=3)
  - Intracerebral bleeding (n=1)



German Registry for Disorders of Eosinophils and Mast Cells (GREM)
Metzgeroth et al., submitted

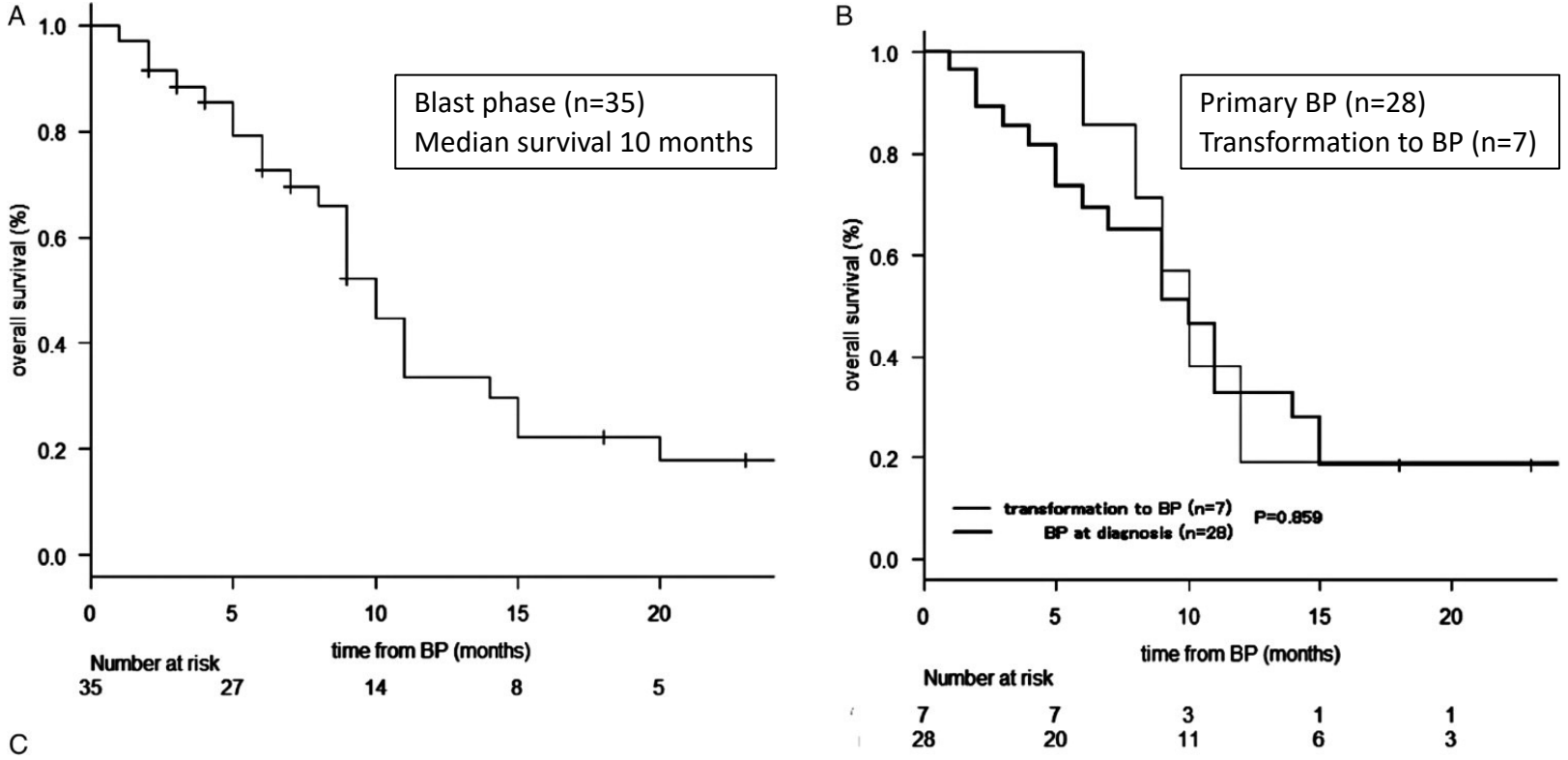
Treatment-free remission in M/LN-eo with *FIP1L1::PDGFRA* fusion



Treatment with imatinib: median 80 months (range, 43-175)
Time in CMR: median 66 months (range, 37-174)

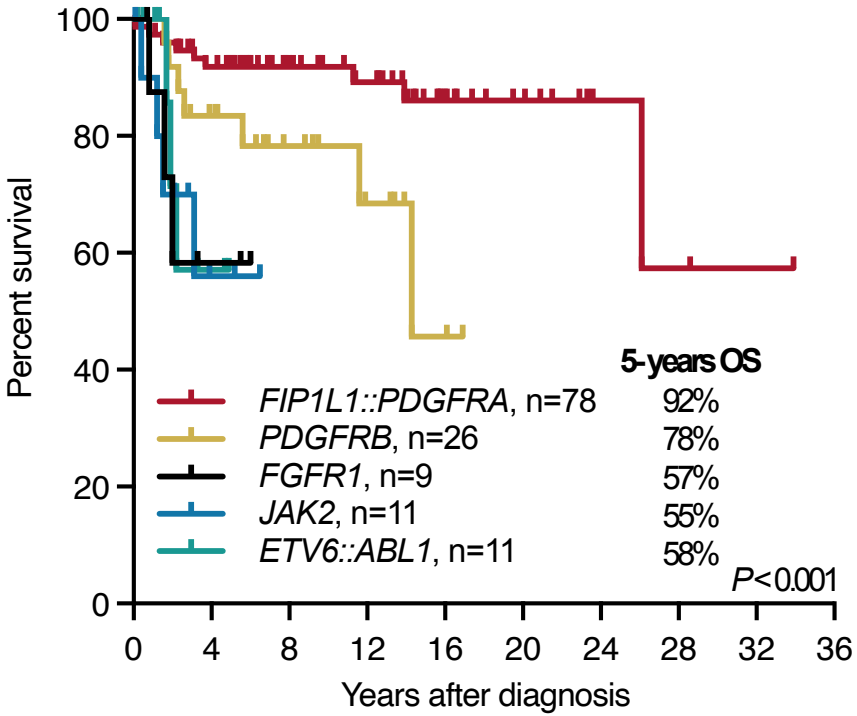
Klion et al., Blood. 2007:110, 4635; Helbig et al. Leukemia Lymphoma. 2016:57, 708,
Qu et al., Oncotarget. 2017:7, 33229; Metzgeroth et al., Blood Advances. 2020:4, 440

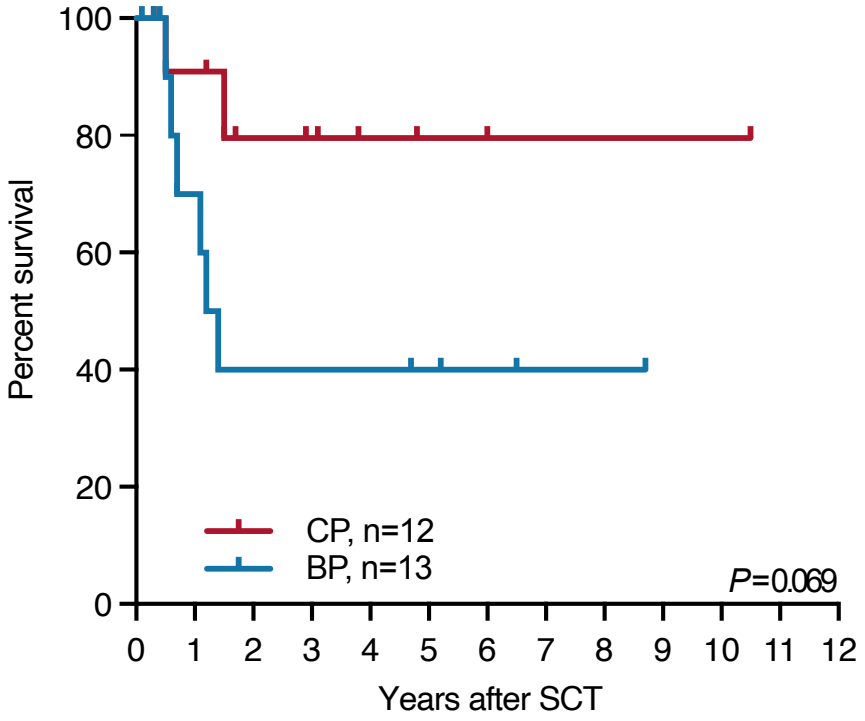
M/LN-eo with *FGFR1* fusions: OS of patients in BP and according to primary or secondary BP



Umino et al., Hematology 23, 470, 2018

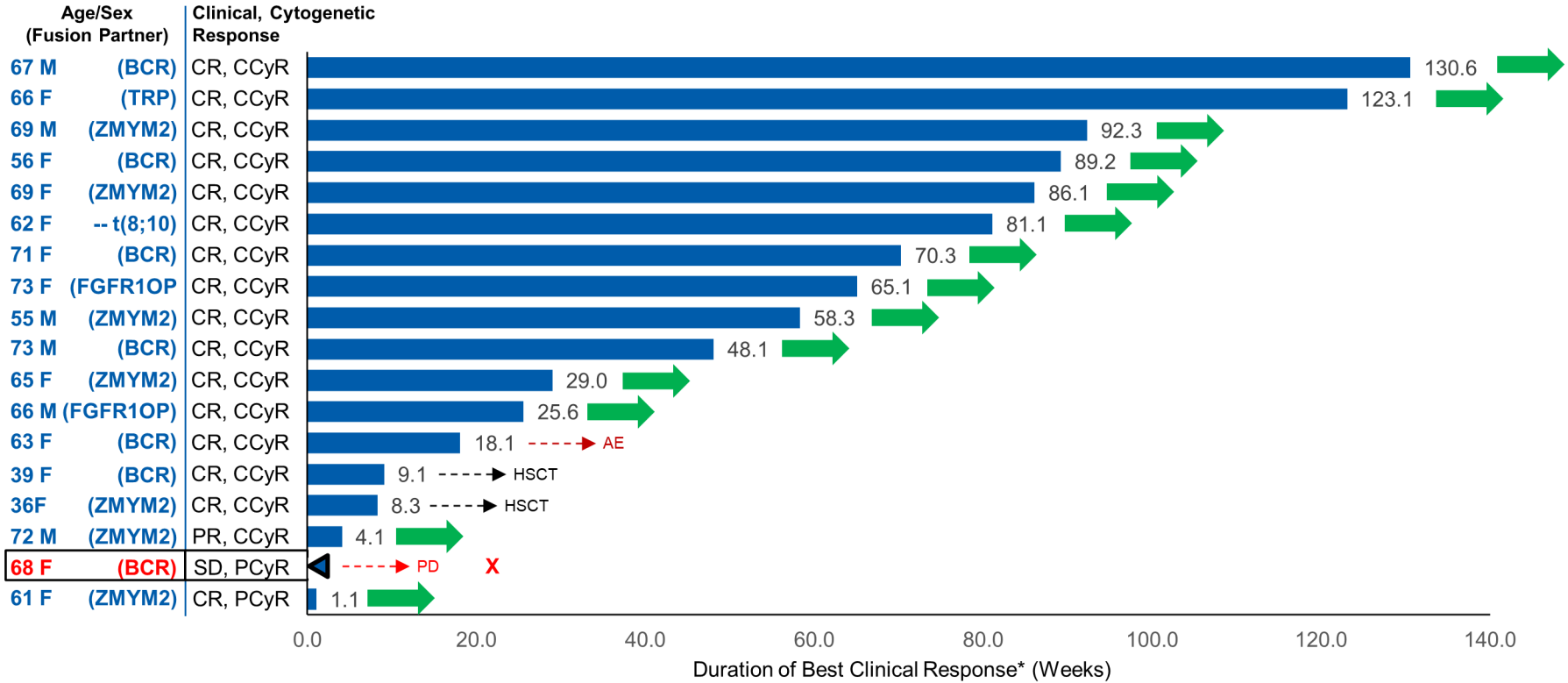
M/LN-eo-TK





German Registry for Disorders of Eosinophils and Mast Cells (GREM)
Metzgeroth et al., submitted

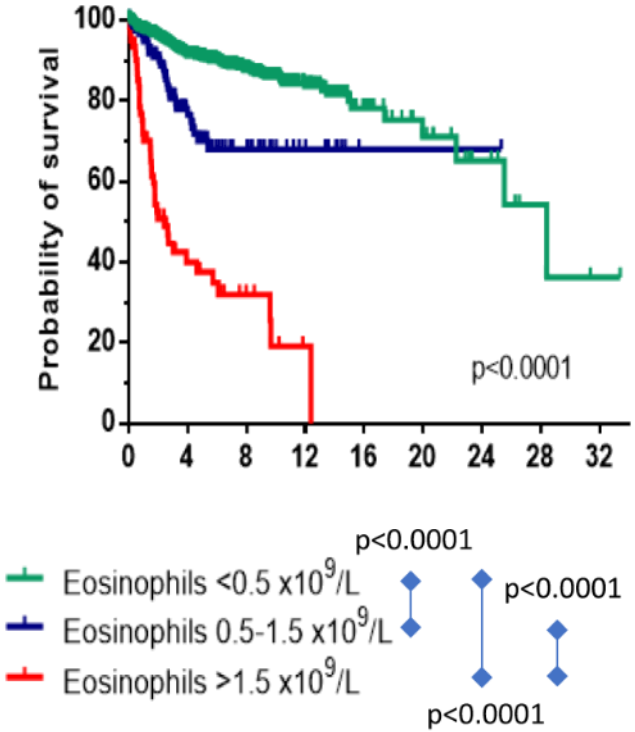
Chronic Phase Disease Only (n=18): Best Clinical and Cytogenetic Responses per CRC



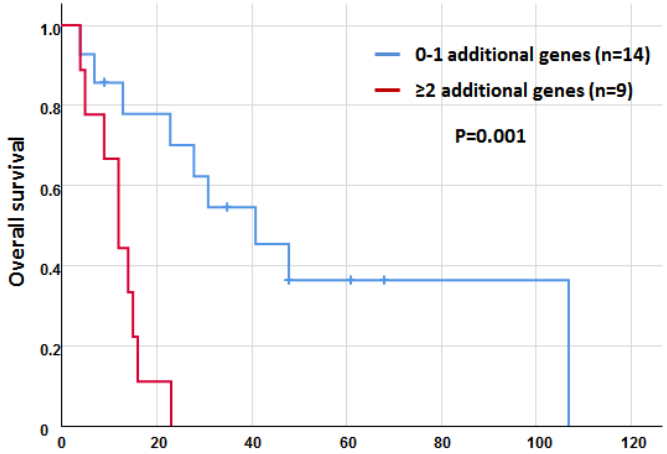
*Swimmer lane representative of duration of clinical response only.
X denotes death; green arrow shows patients still receiving treatment at the time of data cut-off; **Black-outlined** triangle ◀ shows non-responder.
AE, adverse event; CCyR, complete cytogenetic response; CR, complete response; CRC, Central Review Committee; HSCT, hematopoietic stem cell transplant; NE, not evaluable; PR, partial response; SD, stable disease.

Gotlib et al., Presentation at ASH 2021

Survival of eosinophilia in association with point mutations



***KIT* D816V**

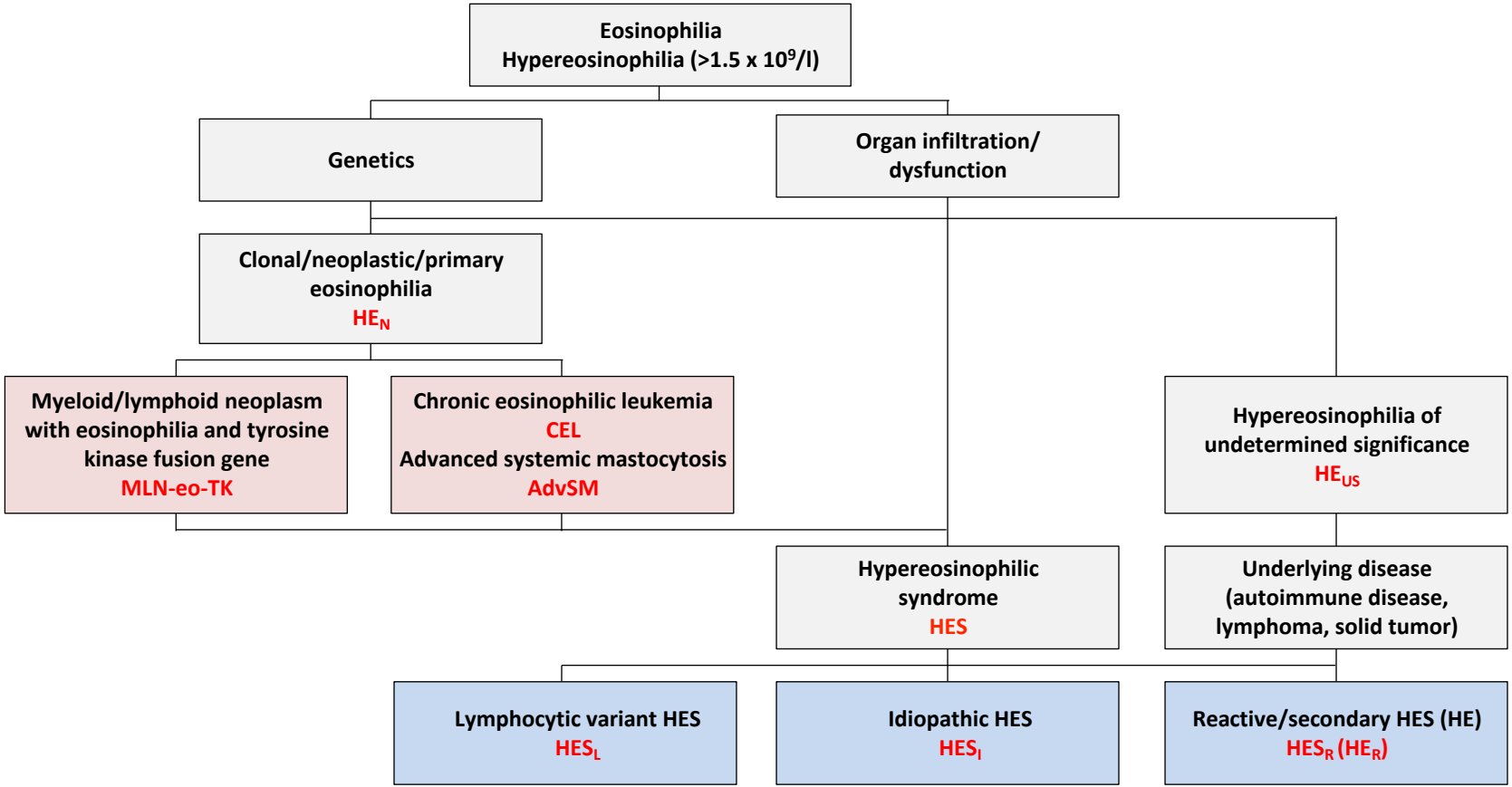


- Identified in 27/1715 (1.6%) patients with eosinophilia
- = CEL-NOS
- Median of 2 (range 0-4) additional myeloid mutations, e.g. *SF3B1*, *SRSF2*, *ASXL1*, *EZH2*, *RUNX1*
- Median overall survival 30 months

***STAT5B* N642H**

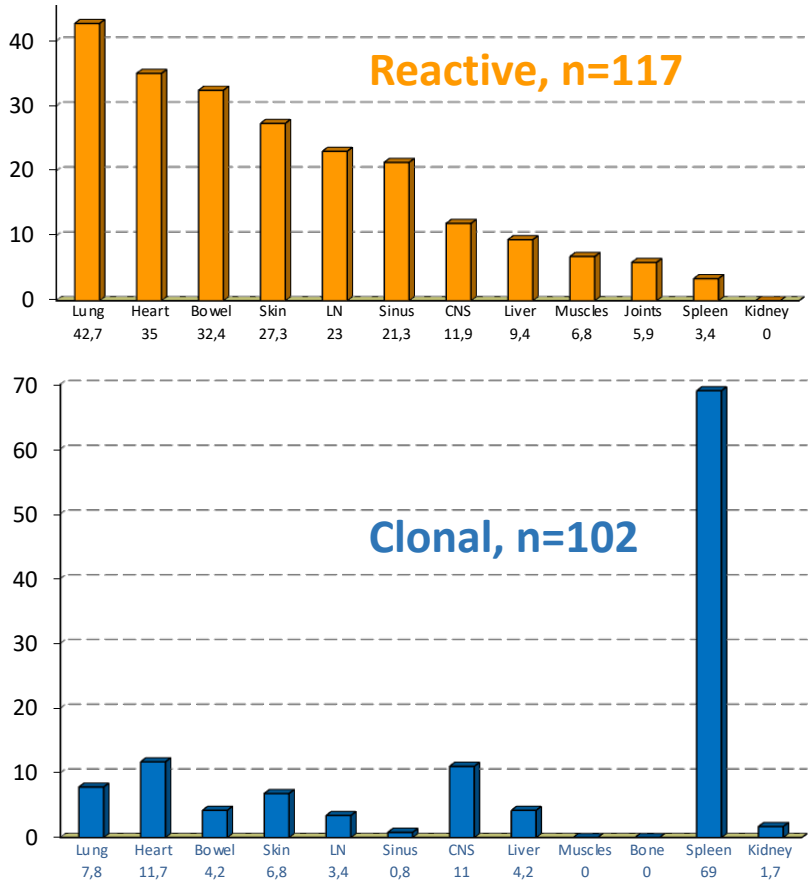
Kluin-Nelemans et al., Leukemia 2020; Cross et al., Leukemia 2019

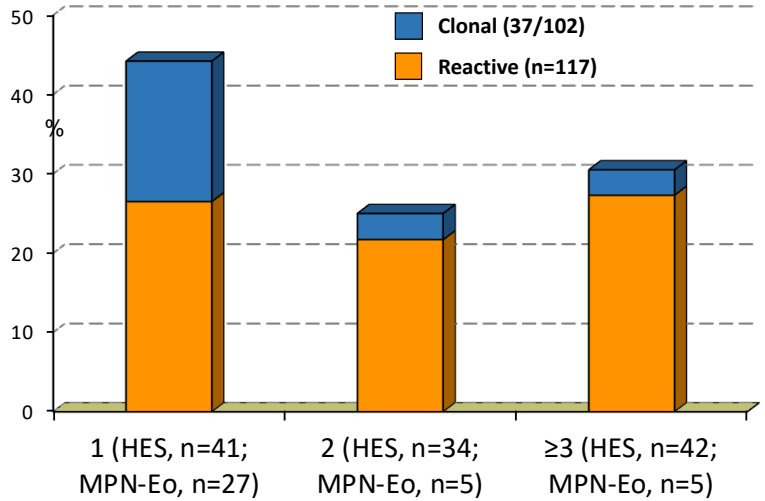
Terminology of eosinophilia-associated disorders



Adapted from Valent et al., JACI 2012

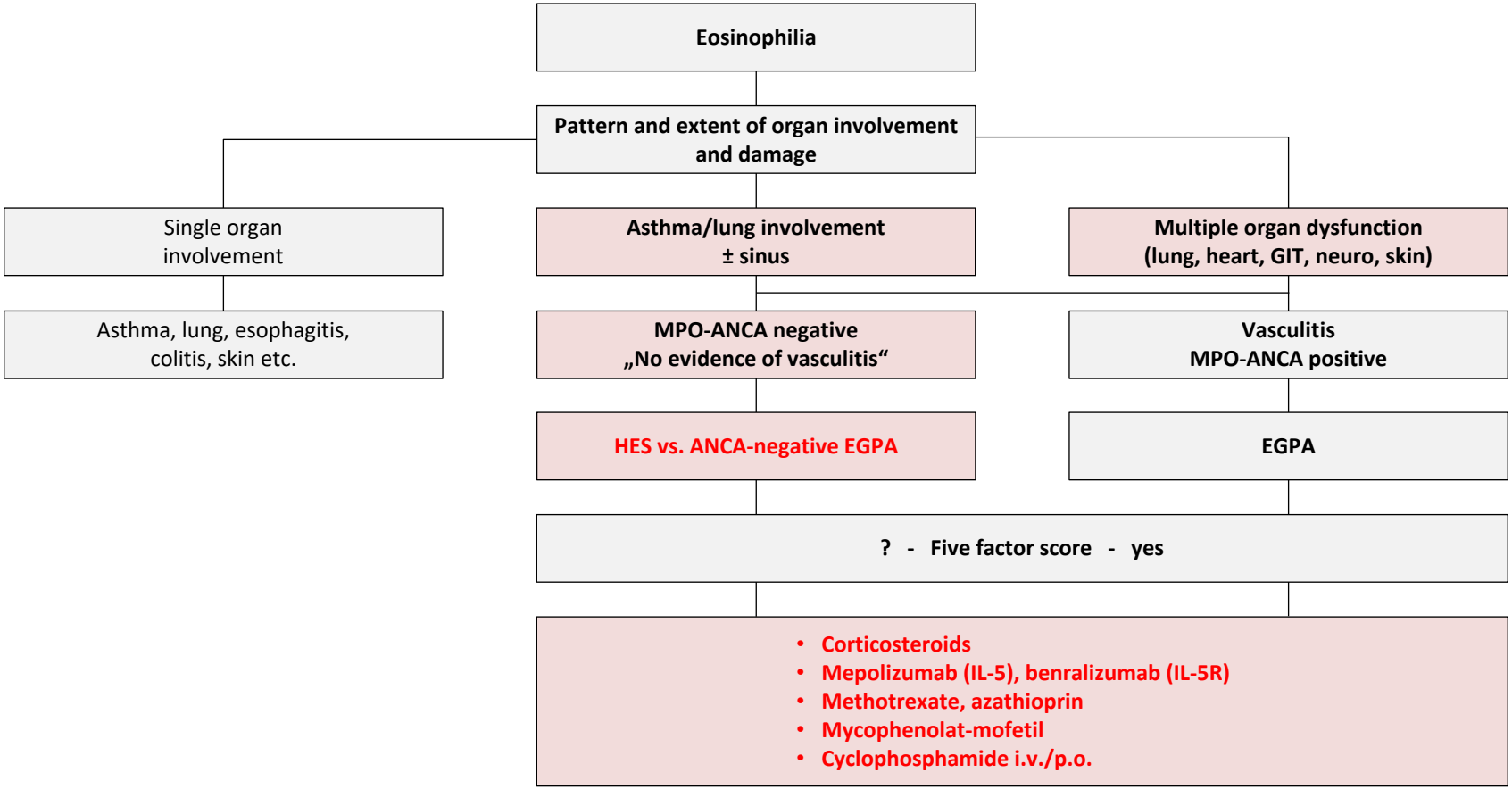
Organ involvement in reactive and clonal eosinophilia





German Registry for Disorders of Eosinophils and Mast Cells (GREM); unpublished data

Eosinophilia and organ damage



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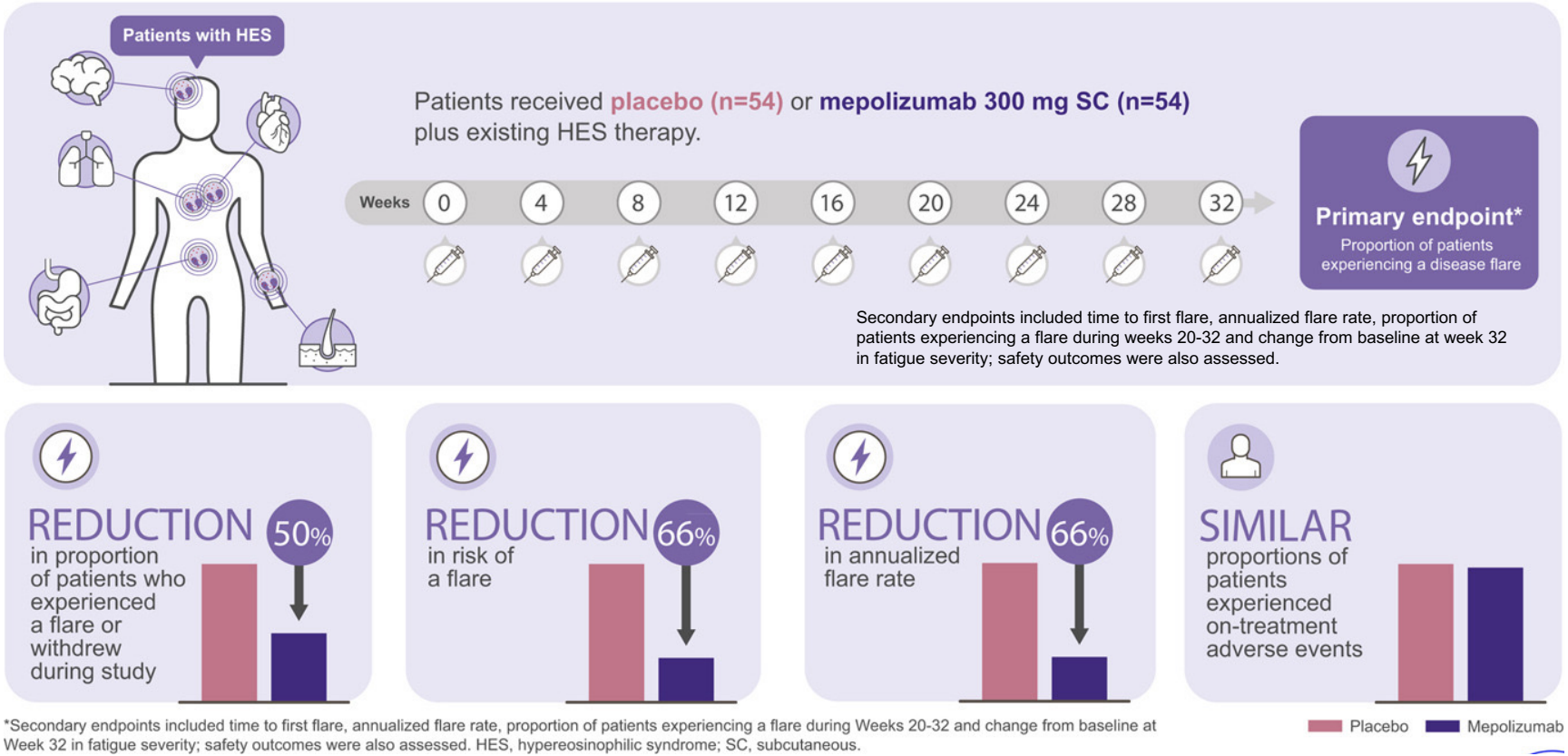
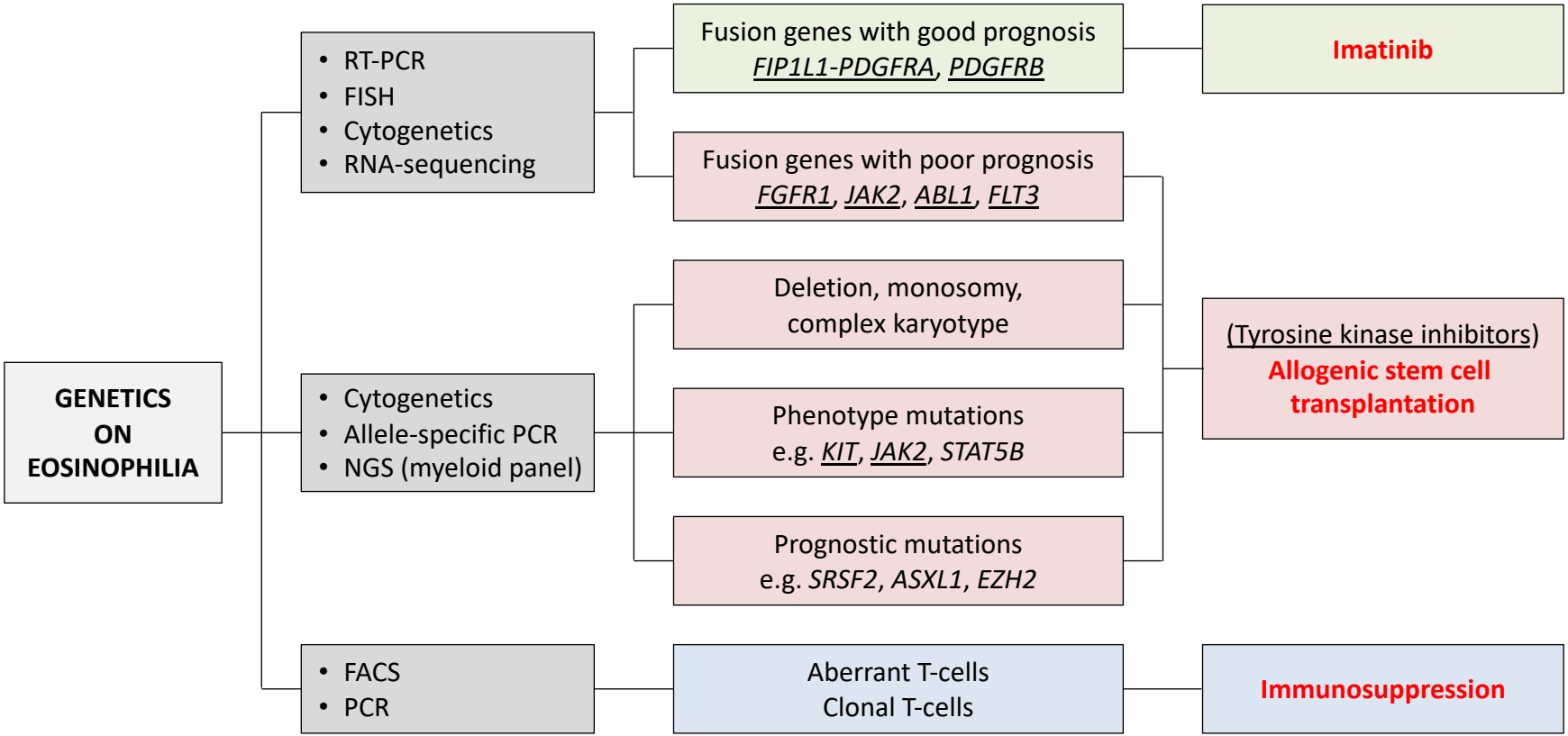
Mepolizumab in HES



*Secondary endpoints included time to first flare, annualized flare rate, proportion of patients experiencing a flare during Weeks 20-32 and change from baseline at Week 32 in fatigue severity; safety outcomes were also assessed. HES, hypereosinophilic syndrome; SC, subcutaneous.

Roufosse et al., J Allergy Clin Immunol 2020

Eosinophilia: complex genetics and its consequences



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