TUMOR ZENTRUM Oberösterreich

Leitlinie

Immunthrombozytopenie (ITP)

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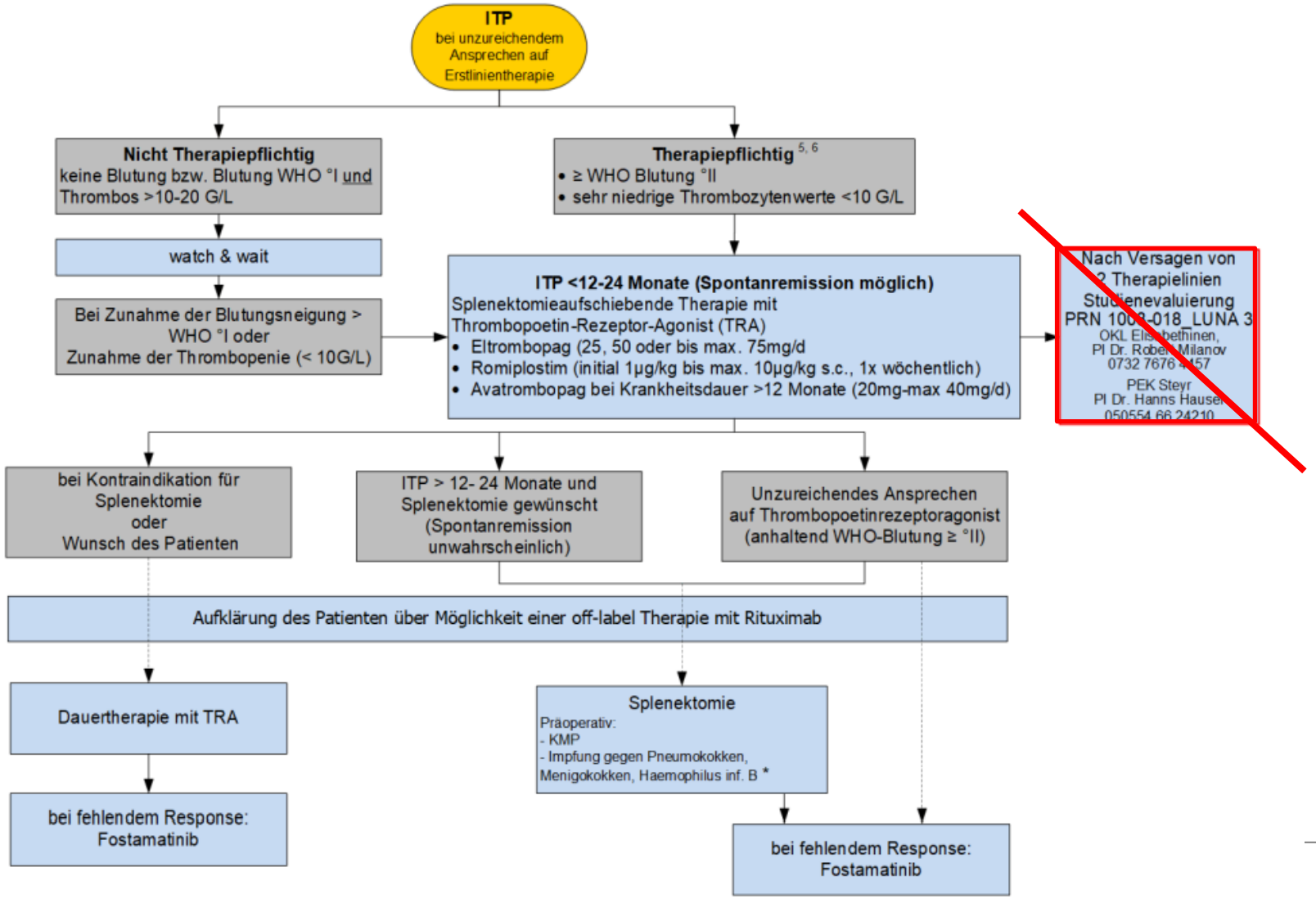
Interne I

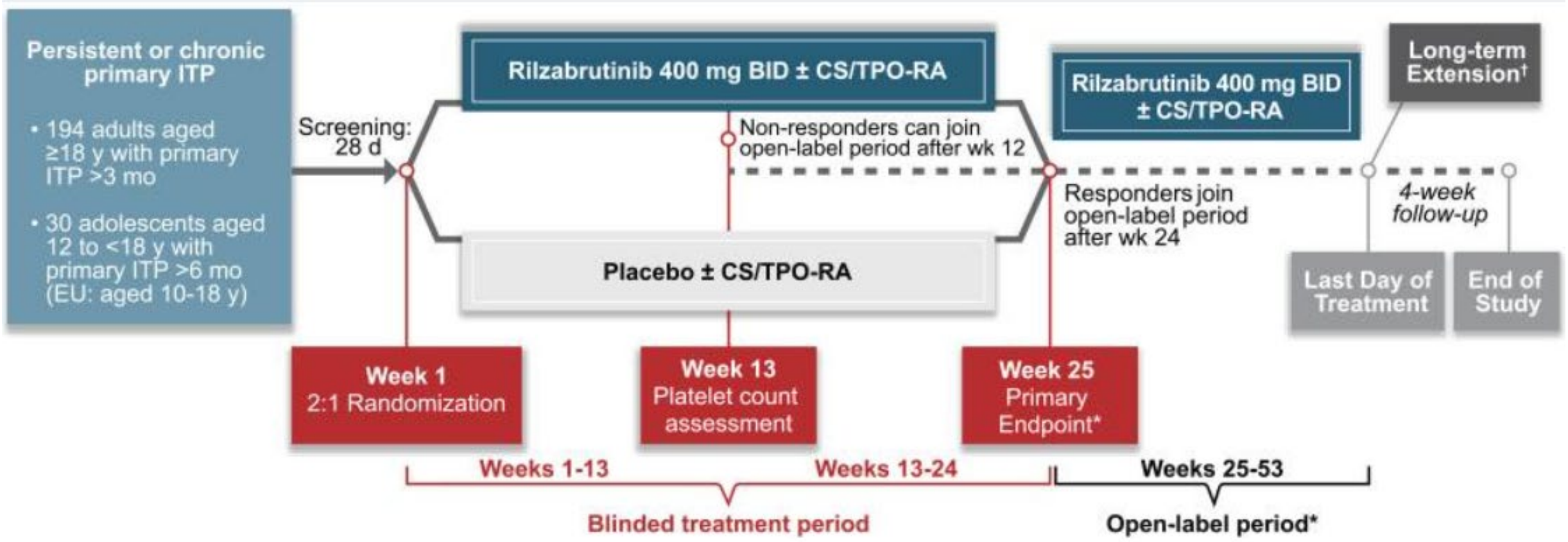
Tumorzentrumstag

Aktuelle Veränderungen der Leitlinie

3.2.2 Zweitlinientherapie



Rilzabrutinib *versus* placebo in adults and adolescents with persistent or chronic immune thrombocytopenia: LUNA 3 phase III study



Rilzabrutinib *versus* placebo in adults and adolescents with persistent or chronic immune thrombocytopenia: LUNA 3 phase III study

- Primary endpoint:
  - Platelet counts ⩾50 × 10^9/L for ⩾two-thirds of ⩾8 available weeks

- Key secondary endpoints
  - Number of weeks with platelet counts ⩾50 × 10^9/L or between ⩾30 × 10^9/L and <50 × 10^9/L
  - Number of weeks with platelet counts ⩾30 × 10^9/L and at least doubled from baseline
  - Time to first platelet counts ⩾50 × 10^9/L or between ⩾30 × 10^9/L and <50 ×10^9 /L and at least doubled from baseline
  - Proportion of patients requiring rescue therapy

- Ergebnisse aus Phase III noch ausständig

- Lt. Phase II Daten response Raten um 40%, bei guter Verträglichkeit

Assessment of thrombotic risk during long-term treatment of immune thrombocytopenia with fostamatinib

- Daten der FIT I/II Studien
- ausgeschlossen waren Pat. mit Factor V Leiden Mutation, APC-Resistenz, AT-III Mangel oder thromboembolischen Ereignis 6 Monate vor Randomisierung
- Verhätnismäßige hohe Zahl an Pat. mit mind. 1 Risikofaktor für TEE (87%)
- Lediglich ein Fall einer milden TIA (0,7%) unter Fostamatinib

Table 1. Baseline patient characteristics and risk factors for thromboembolic events (TEEs).

Baseline characteristics	All patients *N* = 146
Patients with ⩾1 risk factor for TEE, *n* (%)	127 (87)
Patients with multiple risk factors for TEE, *n* (%)	85 (58)
Number of TEE risk factors, median (range)	2 (0–7)
Age ⩾65 years, *n* (%)[a]	37 (25)
Body mass index ⩾30 (%)	43 (29)
Medical history	
Diabetes (%)	15 (10)
Cancer[b] (%)	7 (5)
Cardiovascular disease, excluding hypertension (%)	37 (25)
Hypertension (%)	51 (35)
Prior ITP treatments	
Splenectomy (%)	51 (35)

a Fifteen (10%) males were over age 65 years.

b Breast cancer in three, endometrial cancer in two, colorectal cancer, non-melanoma skin cancer in five.

TUMOR ZENTRUM Oberösterreich

- Keine direkten Vergleiche zu TRA
  - Lt. Studienlage jedoch zumindest höhere Inzidenz

Von 2,2% bis 8,9%

- TEE-Raten pro 100-Pat. Jahren

Eltrombopag vs. Romiplostim vs. Fostamatinib:

-2,7 vs. 3,1 bzw. 3,9 vs. 0,44

Study type and reference	Drug and duration of study	Incidence[a]	No. of events	Type of thromboembolic event
Eltrombopag				
Phase III placebo-controlled study – Bussel *et al.*[54]	Eltrombopag, 6 months	0/76 (0%)	0	None
Phase III placebo-controlled study – Cheng *et al.*[55]	Eltrombopag, 6 months	3/135 (2.2%)	3	Pulmonary embolism (PE), deep vein thrombosis (DVT)
Phase III open-label extension study – Wong *et al.*[46]	Eltrombopag, 8 years	19/302 (6.3%)	24	PE, pulmonary infarction, DVT, myocardial infarctions (MIs), cerebral infarction/ischemia, transient ischemic attack (TIA), thrombophlebitis superficial
Romiplostim				
Two phase III placebo-controlled studies – Kuter *et al.*[58]	Romiplostim, 6 months	2/84 (2.4%)	2	Cerebrovascular accident, right popliteal arterial embolism
Phase III single-arm extension study – Bussel *et al.*[53]	Romiplostim, 3 years	7/142 (4.9%)	12	MI, portal vein thrombosis, DVT, coronary artery occlusion, transverse sinus thrombosis, septic thrombophlebitis, TIA, thrombosis
Phase III extension study – Gernsheimer *et al.*[56]	Romiplostim, 3 years	4/101 (4.0%)	8	Coronary artery occlusion, superficial vein thrombosis, MIs, pulmonary embolism, septic jugular vein thrombosis, inflammatory venous thrombosis, cerebral ischemic attack
Phase III extension study – Kuter *et al.*[48]	Romiplostim, 5 years	19/291 (6.5%)	25	MIs, TIAs, cerebrovascular accidents, hemiparesis, transient blindness, PE, portal vein thrombosis (PVT), DVT, catheter thrombosis, transverse sinus thrombosis, thrombophlebitis
Phase IV open-label studies – Janssens *et al.*[47]	Romiplostim, 3 years	15/169 (8.9%)	21	DVTs, cerebrovascular accidents, PEs, thrombophlebitis superficial and thrombosis PVT, pulmonary thrombosis, ischemic stroke, peripheral embolism, MI, thrombosis

Avatrombopag				
Phase II placebo-controlled and open-label extension – Bussel *et al.*[52]	Avatrombopag, 7 months	4/63 (6.3%)	5	MI, DVT, thrombophlebitis, retinal artery occlusion, stroke
Phase III placebo-controlled study – Jurczak *et al.*[57]	Avatrombopag, 7 months	3/32 (9.4%)	3	DVT, asymptomatic PE, cerebrovascular event
Phase III extension study – Jurczak *et al.*[57]	Avatrombopag, 2 years	1/39 (2.6%)	1	Jugular vein thrombosis

- Ähnliche TEE-Rate unter Avatrombopag im Bereich zwischen 2,6% bis 9,4%

Efficacy and Safety of Intravenous Efgartigimod in Adults with Primary Immune Thrombocytopenia: Results of a Phase 3, Multicenter, Double-Blinded, Placebo-Controlled, Randomized Clinical Trial (ADVANCE IV)

- Einschlußkriterien:
  - Persistierende/chron. ITP
  - Mind. 2 vorausgegangene Therapien
  - Thr. <30 G/L

- 2:1 Randomisierung 10 mg/kg EFG oder PBO für 24 Wochen

- primärer Endpunkt: sustained PLT response (PLT of $\geq 50 \times 10^9$/L)

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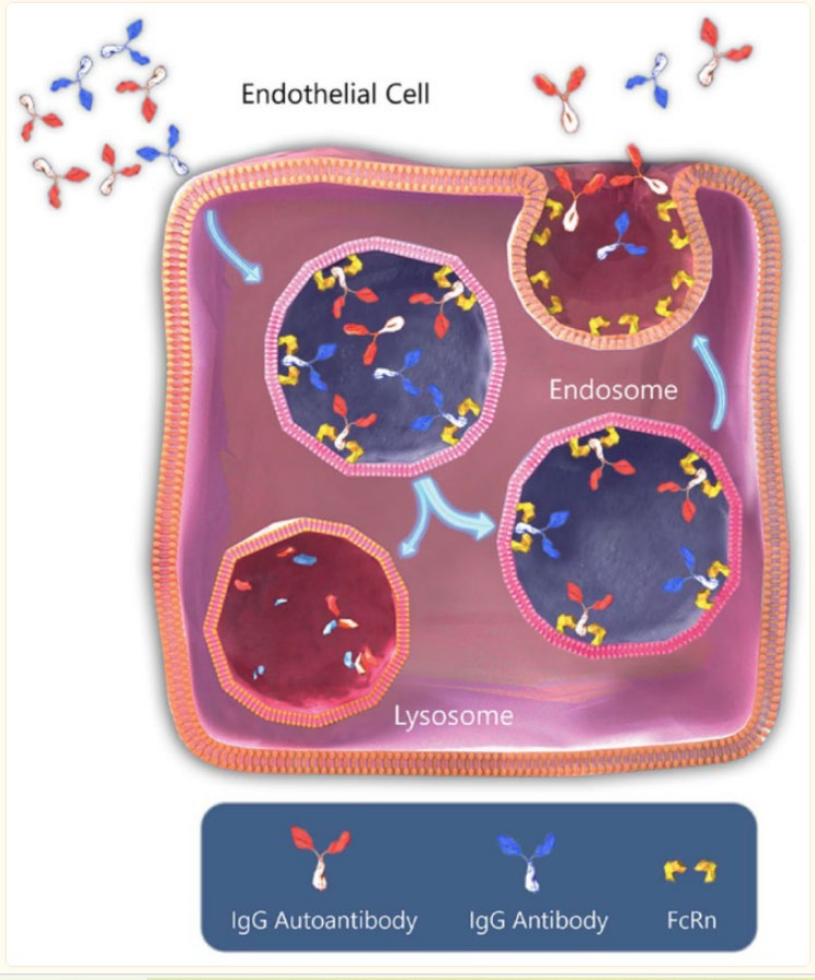
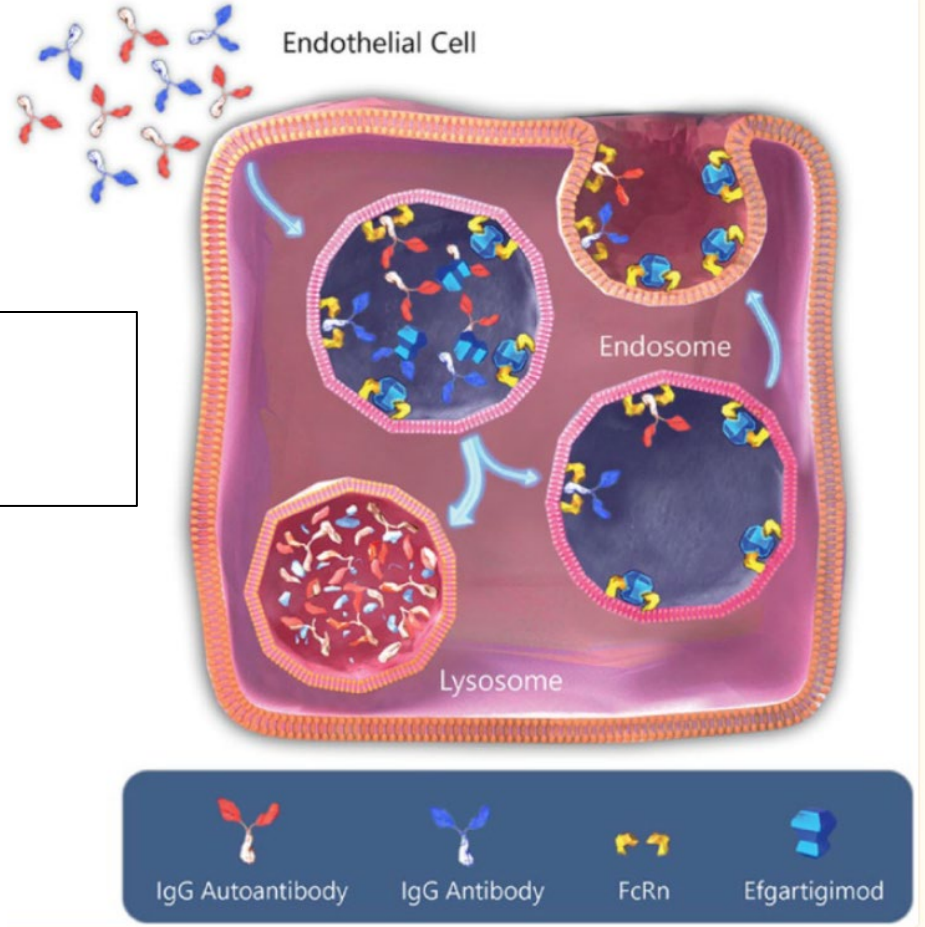


Hemmung von FcRn verhindert IgG-Recycling und führt zur Reduktion von Auto-Ak



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- Patientencharakteristika:

-n=131 (118 chronic ITP, 13 persistent ITP; 86 EFG, 45 PBO)

- lange bestehende, schwere ITP (mediane Zeit seit Diagnose 4.57 Jahre; baseline median PLT um 17×10^9/L)

-schwer vortherapiert(67.2% ≥3 vorangegangene ITP-Therapien)

Efficacy and Safety of Intravenous Efgartigimod in Adults with Primary Immune Thrombocytopenia: Results of a Phase 3, Multicenter, Double-Blinded, Placebo-Controlled, Randomized Clinical Trial (ADVANCE IV)

Advance primary and secondary endpoints.

	Efgartigimod group(86)	Placebo group(45)
Primary endpoint [a] (platelet count > 50×10^9/L in >4/6 visits weeks 19–24 in chronic ITP patients	21.8% (17/78)	5.0% 2/40
Secondary endpoint [a] (number of weeks with platelet count > 50×10^9/L	6.1 weeks	1.5 weeks
Secondary endpoint [b] (platelet count > 50×10^9/L in >4/6 visits in weeks 19/24 all patients	25.6% (22/86)	6.7% 3/45
Secondary endpoint [b] Sustained response for at least 6 weeks	22.1% (19/86)	6.7% (2/45)
Time to response [b] Platelet count of 30×10^9/L by week 1	38.4% (33/86)	11.1% (5/45)

Efficacy and Safety of Intravenous Efgartigimod in Adults with Primary Immune Thrombocytopenia: Results of a Phase 3, Multicenter, Double-Blinded, Placebo-Controlled, Randomized Clinical Trial (ADVANCE IV)

- Safety:
  - Blutungsereignisse 70.9% (61/86) in der Efgartigimod Gruppe vs. 86.7% (39/45) im Kontrollarm.
  - Infektionen in 29.1%. (25/86) in der Efgartigimod Gruppe vs. 22.2% (10/45) im Kontrollarm. Infectionen waren mild bis moderate in beiden Gruppen (trotz Hypogammaglobulinämie im Therapiearm)
  - Infusionsreaktionen bei 11.6% (10/86) in der Efgartigimod Gruppe vs. 11.1% (5/45)

Abstimmung der Leitlinie

Abstimmung durch die Leitliniengruppe

(a) Die Leitlinie wird ohne Einschränkung freigegeben

(b) Die Leitlinie wird nach Umsetzung der protokollierten Inhalte freigegeben

(c) Die Leitlinie wird aufgrund der protokollierten Inhalte / Einwände nicht freigegeben