Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2019-B-283z Fostamatinib

Stand: Januar 2020

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA

Fostamatinib **Primäre Immunthrombozytopenie**	
Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	Splenektomie
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Es liegen keine Beschlüsse vor.
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	*Siehe systematische Literaturrecherche*

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Fostamatinib ATC-Code Handelsname®	Anwendungsgebiet laut Positive Opinion: “Tavlesse is indicated for the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments.” [inoffizielle Übersetzung: „Behandlung der chronischen Immunthrombozytopenie bei erwachsenen Patienten, die refraktär gegenüber anderen Behandlungen sind.“]
Kortikosteroide	
Dexamethason H02AB02 Dexamethason JENAPHARM® Generisch	– […] – Orale Anfangsbehandlung von **Autoimmunerkrankungen**, wie systemischer Lupus erythematodes (insbesondere viszerale Formen), – […] (FI Stand Februar 2018)
Prednisolon H02AB06 Prednisolon JENAPHARM® Generisch	[…] angezeigt zur Behandlung von Erkrankungen, die einer systemischen Therapie mit Glucocorticoiden bedürfen. Hierzu gehören je nach Erscheinungsform und Schweregrad […] <u>Hämatologie/Onkologie:</u> – autoimmunhämolytische Anämie, Idiopathische thrombozytopenische Purpura (Morbus Werlhof), akute intermittierende Thrombozytopenie – […] (FI Stand Juni 2018)
Methylprednisolon H02AB04 Methylprednisolon JENAPHARM® Generisch	Erkrankungen, die einer systemischen Therapie mit Glukokortikoiden bedürfen. Hierzu gehören je nach Erscheinungsform und Schweregrad zum Beispiel: […] <u>Blutkrankheiten/Tumorerkrankungen</u> – Autoimmunhämolytische Anämie
Prednison H02AB07	[…] angezeigt zur Behandlung von Erkrankungen, die einer systemischen Therapie mit Glucocorticoiden bedürfen. Hierzu gehören je nach Erscheinungsform und Schweregrad […]

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Prednison acis® Generisch	Hämatologie/Onkologie: – autoimmunhämolytische Anämie, Idiopathische thrombozytopenische Purpura (Morbus Werlhof), akute intermittierende Thrombozytopenie – […] (FI Stand August 2017)
Weitere Wirkstoffe	
Immunoglobuline J06BA02 Flebogamma DIF®	[…] Immunmodulation bei Erwachsenen, Kindern und Jugendlichen (2 – 18 Jahre) bei: – Primärer Immunthrombozytopenie (ITP) bei Patienten mit hohem Blutungsrisiko oder vor Operationen zur Korrektur der Thrombozytenzahl. (FI Stand Oktober 2018)
Humanes Thrombozyten-konzentrat	Die Gabe von Thrombozytenkonzentraten ist indiziert zur Behandlung einer Blutungsneigung, bedingt durch eine schwere Thrombozytopenie infolge thrombozytärer Bildungsstörungen, im Notfall auch bei Umsatzstörungen, jedoch nicht bei einer niedrigen Thrombozytenzahl allein. Damit durch die Zufuhr von Plättchen eine Besserung der thrombozytär bedingten Blutungsneigung zu erwarten ist, sollte vor der Behandlung zunächst deren Ursache abgeklärt werden. (FI Stand September 2013)
Eltrombopag B02BX05 Revolade®	Revolade ist für die Behandlung von Patienten im Alter von 1 Jahr und älter mit primärer Immunthrombozytopenie (ITP) indiziert, wenn diese 6 Monate oder länger nach Diagnosestellung andauert und die Patienten gegenüber anderen Therapien refraktär sind (z. B. Kortikosteroide, Immunglobuline) (siehe Abschnitte 4.2 und 5.1). (FI Stand Februar 2019)
Romiplostim B02BX04 Nplate®	Nplate ist für die Behandlung von Patienten mit chronischer immun-(idiopathischer) thrombozytopenischer Purpura (ITP) im Alter von 1 Jahr oder älter indiziert, die gegenüber anderen Therapien refraktär sind (z. B. Kortikosteroide, Immunglobuline; siehe Abschnitte 4.2 und 5.1) (FI Stand Januar 2018)
Azathioprin Azathioprin acis® generisch	[…] angezeigt in schweren Fällen der folgenden Erkrankungen zur Reduktion der Corticoid-Dosis oder bei Patienten, die Corticoide nicht vertragen bzw. bei denen mit hohen Dosen von Corticoiden keine ausreichende therapeutische Wirkung erzielt werden kann: […] – chronisch refraktäre idiopathische thrombozytopenische Purpura […] (FI Stand September 2017)

Quellen: AMIS-Datenbank, Fachinformationen (Stand: Dezember 2019)

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2019-B-283z (Fostamatinib)

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	10. Dezember 2019

Inhaltsverzeichnis

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
ELT	Eltrombopag versus romiplostim
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
HR	Hazard Ratio
ITP	Immunthrombozytopenie
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KI	Konfidenzintervall
LoE	Level of Evidence
NICE	National Institute for Health and Care Excellence
OR	Odds Ratio
ROM	Romiplostim
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
TPO-RAs	Thrombopoietin-receptor agonists
WHO	World Health Organization

1 Indikation

Tavlesse is indicated for the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation Immunthrombozytopenie durchgeführt. Der Suchzeitraum wurde auf die letzten 5 Jahre eingeschränkt und die Recherche am 06.05.2019 abgeschlossen. Die Suche erfolgte in den aufgeführten Datenbanken bzw. Internetseiten folgender Organisationen: The Cochrane Library (Cochrane Database of Systematic Reviews), MEDLINE (PubMed), AWMF, G-BA, GIN, NICE, TRIP, SIGN, WHO. Ergänzend erfolgte eine freie Internetsuche nach aktuellen deutschen und europäischen Leitlinien. Die detaillierte Darstellung der Suchstrategie ist am Ende der Synopse aufgeführt.

Die Recherche ergab 242 Quellen, die anschließend in einem zweistufigen Screening-Verfahren nach Themenrelevanz und methodischer Qualität gesichtet wurden. Zudem wurde eine Sprachrestriktion auf deutsche und englische Quellen vorgenommen. Insgesamt ergab dies 3 Quellen, die in die synoptische Evidenz-Übersicht aufgenommen wurden.

3 Ergebnisse

3.1 G-BA Beschlüsse/IQWiG Berichte

Es liegen keine Beschlüsse vor.

3.2 Cochrane Reviews

Es konnten keine relevanten CR im vorliegenden AWG identifiziert werden.

3.3 Systematische Reviews

Elgebaly AS et al., 2017 [1].

Tolerability and efficacy of eltrombopag in chronic immune thrombocytopenia: meta-analysis of randomized controlled trials

Fragestellung

The aim of this meta-analysis is to synthesize evidence from published randomized controlled trials (RCTs) about the safety and efficacy of eltrombopag for both adult and children with ITP.

Methodik

Population:

- patients having chronic ITP

Intervention:

- Eltrombopag

Komparator:

- Placebo

Endpunkte:

- overall platelet response defined as platelet counts of at least 50 x 109/L in the absence of rescue therapy, incidence of significant bleeding (WHO grades II-IV) according to WHO bleeding scale, incidence of any bleeding (WHO grades I-IV), number of cases needed to rescue treatment, and adverse events

Recherche/Suchzeitraum:

- PubMed, Scopus, Web of Science, and Cochrane Central
- Zeitraum: k.A.

Qualitätsbewertung der Studien:

- The quality of the retrieved RCTs was assessed according to Cochrane Handbook of Systematic Reviews of Interventions

Ergebnisse

Anzahl eingeschlossener Studien:

- 6 RCTs (N=611 patients)

Charakteristika der Population:

- population was patients (adults or children) with a clinical diagnosis ofchronic ITP and a platelet count less than 30 x 10^9/L

Qualität der Studien:

- The quality of the included studies was from moderate to high quality according to the Cochrane risk of bias assessment tool.

Studienergebnisse:

- Efficacy analysis.
  - Overall effect estimate favored eltrombopag group in terms of the overall platelet response (RR = 3.42; 95% CI [2.51-4.65]; P < .0001), pooled studies were homogenous (I^2 = 22%; P = .27);
  - incidence of significant bleeding (WHO grades II-IV; RR = 0.56; 95% CI: 0.41-0.77; P = .0004), pooled studies were homogenous (I^2 = 0%; P = .40);
  - number of cases needed to rescue treatment (RR = 0.45; 95% CI: 0.32-0.65; P < .0001), pooled studies were homogenous (I^2 = 38%; P = .20);
  - incidence of any bleeding (RR = 0.74; 95% CI: 0.66-0.83; P < .00001); I^2 = 0%; P = .48
- adverse events
  - total number of adverse events reported in both groups did not differ significantly; the frequency of adverse events was not higher in the eltrombopag group when compared to placebo (RR: 0.95; 95% CI [0.871.05]; P = .32).
  - Thromboembolic events: Among the 6 included studies, only RAISE and Tomiyama et al studies reported the occurrence of thromboembolic events in eltrombopag group, 2% and 7% (1 patient), respectively. All remaining studies stated that no thromboembolic events were recorded during the course of the study.

Anmerkung/Fazit der Autoren

Eltrombopag is a tolerable and effective drug for the management of chronic ITP in children and adults.

Kommentare zum Review

Patientenpopulation: Kinder und Erwachsene eingeschlossen

Zhang J et al., 2018 [3].

Eltrombopag versus romiplostim in treatment of adult patients with immune thrombocytopenia: a systematic review incorporating an indirect-comparison meta-analysis

Fragestellung

Therefore, this study aims to evaluate the efficacy and safety of ELT versus ROM for adultpatients with ITP using an indirect-comparison meta-analysis.

Methodik

Population:

- Participants were adult (≥ 18 years) with ITP

Intervention:

- thrombopoietin-receptor agonists (ELT or ROM irrespective of dosage and schedule)

Komparator:

- placebo

Endpunkte:

- overall platelet response (primary outcome), defined as achieving at least once platelet response (≥ 50×109/L) during treatment; incidence of overall and serious adverse events (SAEs); durable platelet response, defined as maintaining platelet counts ≥ 50×109/L for at least 60% ofthe duration of TPO-RAs treatment or for six or more weeks during the final eight weeks of TPO-RAs treatment; incidence of clinically significant bleeding (WHO Grade 2–4 or rated as severe, life threatening, or fatal); all bleeding events; and proportion of patients who received rescue treatment

Recherche/Suchzeitraum:

- PubMed, Embase and Cochrane Library, Clinical Trials.gov, China National Knowledge Infrastructure, and Chinese Biomedical Literature Database
- earliest records to May 2017

Qualitätsbewertung der Studien:

- checklist developed by Cochrane Collaboration

Ergebnisse

Anzahl eingeschlossener Studien:

- 9 RCTs (786 participants)

Charakteristika der Population:

- All patients were aged ≥18 years old, with disease duration more than 3 months and baseline platelet count less than 30×109/L.

Qualität der Studien:

- seven studies had low risk of selection bias for central randomization while the other two was unclear because the method of randomization and allocation concealment were not reported
- All studies had low risk of performance bias and detection bias, as both patients and study personnel were masked.
- All studies had low risk of attrition bias, as there was no loss to follow-up or the missing data were dealt with properly (e.g. applying ITT analysis which underestimated the efficacy of the medication).
- All studies had low risk of reporting bias since they were registered in ClinicalTrials. gov and had reported all predesigned outcomes.
- Considering all studies supported by pharmaceutical industry, the bias caused by conflict of interest was unclear.

Studienergebnisse:

- Five studies (606 patients) evaluated the efficacy and safety of ELT in comparison to placebo

- Four studies (180 patients) evaluated the efficacy and safety of ROM
- Overall platelet response
  - was reported in all studies (five for ELT and four for ROM) including 785 patients (ITT).
  - the heterogeneity was not statistically significant (I^2 = 32%, P = 0.21 and I^2 = 4%, P = 0.37, respectively).
  - The pooled results with a fixed-effect model showed that proportion of patients achieving overall response was significantly higher in the TPO-RAs group than in the placebo group (RR = 4.07, 95%CI: 2.91–5.70 for ELT and RR = 8.81, 95%CI: 4.01–19.35 for ROM, respectively).
  - However, the result ofindirect comparison indicated that the overall response between ELT and ROM was not significantly different (RR = 0.59, 95%CI: 0.24–1.45).
- Safety
  - Eight studies (764 participants) reported the overall incidence of any AEs reported in patients receiving TPO-RAs or placebo.
  - The pooled analysis showed that the incidence was not significantly different between two groups (RR = 1.05, 95%CI: 0.84–1.32 for ELT and RR = 1.05, 95%CI: 0.97–1.14 for ROM).
  - And the result of indirect comparison also showed that the overall incidence ofany AEs in ELT group was similar to that in ROM group (RR = 0.98, 95%CI: 0.79–1.21).

Anmerkung/Fazit der Autoren

Eltrombopag and romiplostim might be equivalent in efficacy and safety for adult ITP, however, physicians should still take into account drug cost and comorbidities of the specific patient while making decisions on the treatment of ITP with TPO-RAs.

Wang J et al., 2018 [2].

Efficacy and safety of the combination treatment of rituximab and dexamethasone for adults with primary immune thrombocytopenia (ITP): a meta-analysis

Fragestellung

To conduct a meta-analysis, assessing the efficacy and safety of the combination treatment of dexamethasone and rituximab for adults with ITP (primary immune thrombocytopenia).

Methodik

Population:

- patients with ITP

Intervention:

- rituximab and dexamethasone combination treatment (RTX+DXM)

Komparator:

- dexamethasone monotherapy (DXM)

Endpunkte:

- OR (overall response) rate, CR (complete response) rate, PR (partial response) rate, SR (sustained response) rate, R (relapse) rate, change in Treg cell count (mean [SD]), and AE (adverse event)

Recherche/Suchzeitraum:

- Pubmed, Embase, Cochrane, China National Knowledge (CNKI), Wanfang database, and Sino Med.
- Suchzeitraum: k.A.

Qualitätsbewertung der Studien:

- GRADE pro scale (Grading of Recommendations Assessment, Development and Evaluation) was used to assess the quality of the evidence

Ergebnisse

Anzahl eingeschlossener Studien:

- 11 RCTs

Charakteristika der Population:

- Participants <18 years old.

Qualität der Studien:

- None of the 11 trials was stopped early or funded by industry.
- Adequate randomization was reported by all of the selected trials, with only three trials specifying the randommethod.
- A total of 19 outcomes were assessed by GRADE pro software, ofwhich 32% (6/19) was scaled as high level, 47% (9/19) was moderate level, and 21% (4/19) was low level

Studienergebnisse:

- Overall Response Rate
  - The comparison of OR rate at week 4 was conducted in six trials (n=435).
  - OR rate was significantly higher in combination arm than that in monotherapy arm (RR=1.23, 95% CI: 1.03-1.48, and P=0.03).
  - However, high heterogeneity was found in pooled analysis (P=0.01, I^2=65%)
- Complete Response Rate
  - Six studies (n=435) reported the CR rate at week 4 without significant heterogeneity (P=0.10, I^2=45%).
  - Pooled analysis by using a Fixed-effect model showed that CR rate at week 4 in combination arm was significantly higher than that in monotherapy arm (RR=2.06, 95% CI: 1.63-2.62, and P<0.00001)
- Partial Response Rate
  - PR rate at week 4 was reported by six studies (n=435), pooled analysis of which turned out homogenous (P=0.27, I^2=22%).

- Analysis conducted by a Fixed-effect model showed that PR rate at week 4 in monotherapy arm was significantly higher than that in combination arm (RR=0.66, 95% CI: 0.49-0.88, P=0.005)

- Sustained Response Rate
  - SR rate at month 6 (n=296) and month 12 (n=274) was reported by three studies, respectively, both of which showed no significant heterogeneity (P=0.76, I2=0%; P=0.15, I^2=47%).

- Safety Profile
  - Only three trials (n=286) reported serious AE. Through a Fixed-effect method, no heterogeneity was observed (P=0.67, I^2=0%), and no significant difference was found either (RR=1.93, 95% CI: 1.00-3.71, and P=0.05)

Anmerkung/Fazit der Autoren

Dexamethasone combined with rituximab can provide a better long-term response in the treatment of adults with ITP and will not increase the risk of adverse effects.

Kommentare zum Review

Zulassung: Rituximab off label, Dexamethason unklar

3.4 Leitlinien

Es konnten keine evidenzbasierten Leitlinien im vorliegenden AWG identifiziert werden.

3.5 Ergänzende Dokumente anderer Organisationen zu möglichen Komparatoren

Es konnten keine ergänzenden Dokumente im vorliegenden AWG identifiziert werden.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 5 of 12, May 2019) am 02.05.2019

#	Suchfrage
1	MeSH descriptor: [Purpura, Thrombocytopenic, Idiopathic] explode all trees
2	(idiopathic OR immune OR autoimmune OR (auto NEXT immune) OR autoantibod* OR (auto NEXT antibod*) OR primary):ti,ab,kw
3	(thrombocytopeni* OR thrombocytopaeni*):ti,ab,kw
4	(werlhof* OR ITP):ti,ab,kw
5	#1 OR (#2 AND #3) OR #4
6	#5 with Cochrane Library publication date from May 2014 to May 2019, in Cochrane Reviews

Systematic Reviews in Medline (PubMed) am 02.05.2019

#	Suchfrage
1	purpura, thrombocytopenic, idiopathic[mh]
2	(idiopathic[Title/Abstract] OR immune[Title/Abstract] OR autoimmune[Title/Abstract] OR auto-immune[Title/Abstract] OR autoantibod*[Title/Abstract] OR auto-antibod*[Title/Abstract] OR primary[Title/Abstract])
3	(thrombocytopeni*[Title/Abstract] OR thrombocytopaeni*[Title/Abstract])
4	(werlhof*[Title/Abstract] OR ITP[Title/Abstract])
5	#1 OR (#2 AND #3) OR #4
6	(#5) AND (((Meta-Analysis[ptyp] OR systematic[sb] OR ((systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])) OR Technical Report[ptyp]) OR (((((trials[tiab] OR studies[tiab] OR database*[tiab] OR literature[tiab] OR publication*[tiab] OR Medline[tiab] OR Embase[tiab] OR Cochrane[tiab] OR

	Pubmed[tiab])) AND systematic*[tiab] AND (search*[tiab] OR research*[tiab]))) OR ((((((((((HTA[tiab]) OR technology assessment*[tiab]) OR technology report*[tiab]) OR (systematic*[tiab] AND review*[tiab])) OR (systematic*[tiab] AND overview*[tiab])) OR meta-analy*[tiab]) OR (meta[tiab] AND analyz*[tiab])) OR (meta[tiab] AND analys*[tiab])) OR (meta[tiab] AND analyt*[tiab]))) OR (((review*[tiab]) OR overview*[tiab]) AND ((evidence[tiab]) AND based[tiab]))))))
7	(#6) AND ("2014/05/01"[PDAT] : "3000"[PDAT])

Leitlinien in Medline (PubMed) am 02.05.2019

#	**Suchfrage**
1	purpura, thrombocytopenic, idiopathic[mh]
2	(idiopathic[Title/Abstract] OR immune[Title/Abstract] OR autoimmune[Title/Abstract] OR auto-immune[Title/Abstract] OR autoantibod*[Title/Abstract] OR auto-antibod*[Title/Abstract] OR primary[Title/Abstract])
3	(thrombocytopeni*[Title/Abstract] OR thrombocytopaeni*[Title/Abstract])
4	(werlhof*[Title/Abstract] OR ITP[Title/Abstract])
5	#1 OR (#2 AND #3) OR #4
6	(#5) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR guideline*[ti] OR recommendation*[ti])
7	(#6) AND ("2014/05/01"[PDAT] : "3000"[PDAT])

Referenzen

1. **Elgebaly AS, Ashal GE, Elfil M, Menshawy A.** Tolerability and efficacy of eltrombopag in chronic immune thrombocytopenia: meta-analysis of randomized controlled trials. Clin Appl Thromb Hemost 2017;23(8):928-937.
2. **Wang J, Li Y, Wang C, Zhang Y, Gao C, Lang H, et al.** Efficacy and safety of the combination treatment of rituximab and dexamethasone for adults with primary immune thrombocytopenia (ITP): a meta-analysis. Biomed Res Int 2018;2018:1316096.
3. **Zhang J, Liang Y, Ai Y, Li X, Xie J, Li Y, et al.** Eltrombopag versus romiplostim in treatment of adult patients with immune thrombocytopenia: a systematic review incorporating an indirect-comparison meta-analysis. PLoS One 2018;13(6):e0198504.