Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

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

Vorgang: 2018-B-194-Lusutrombopag

Stand: November 2018

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

Lusutrombopag
[zur Behandlung einer schweren Thrombozytopenie bei Pat. ≥ 18 J. mit chron. Lebererkrankung, die sich invasiver Prozedur unterziehen]

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.	Nicht angezeigt
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:	
Lusutrombopag B02BX07	Anwendungsgebiet laut Zulassung: Lusutrombopag ist indiziert für die Behandlung einer schweren Thrombozytopenie bei erwachsenen Patienten mit einer chronischen Lebererkrankung, die sich einer invasiven Prozedur unterziehen
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)

Quellen: AMIS-Datenbank, Fachinformationen. Stand November 2018.

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

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

Vorgang: 2018-B-194 (Lusutrombopag)

Auftrag von:	Abt. AM
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Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
HR	Hazard Ratio
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
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Lusutrombopag ist indiziert zur Behandlung einer schweren Thrombozytopenie bei erwachsenen Patienten mit einer chronischen Lebererkrankung, die sich einer invasiven Prozedur unterziehen.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen, HTA-Berichten und evidenzbasierten systematischen Leitlinien zur Indikation *Thrombozytopenie bei chronischer Lebererkrankung* durchgeführt. Der Suchzeitraum wurde auf die letzten 5 Jahre eingeschränkt und die Recherche am 18.09.2018 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, IQWiG, 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 920 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 im vorliegenden AWG vor.

3.2 Cochrane Reviews

Estcourt LJ et al., 2018 [1].

Prophylactic platelet transfusions prior to surgery for people with a low platelet count

Fragestellung

To determine the clinical effectiveness and safety of prophylactic platelet transfusions prior to surgery for people with a low platelet count.

Methodik

Population:

- People of all ages with a low platelet count who were due to have surgery including invasive procedures.

Intervention/Komparator:

- Comparison 1: prophylactic platelet transfusion prior to surgery versus no prophylactic platelet transfusion prior to surgery (placebo or no treatment).
- Comparison 2: prophylactic platelet transfusion prior to surgery versus alternative treatments (cryosupernatant, antifibrinolytics, TPO mimetics).
- Comparison 3: different platelet count thresholds for administering a prophylactic platelet transfusion prior to surgery.

Endpunkte:

Primary outcomes

- Mortality (all-causes, secondary to bleeding, secondary to thromboembolism and secondary to infection) within 30 days and 90 days of surgery.
- Number of participants with major procedure-related bleeding within seven days of surgery, defined as:
  - surgical site bleeding requiring a second intervention or reoperation or surgical site bleeding that causes a haematoma or haemarthrosis of sufficient size to delay mobilisation or wound healing;
  - bleeding of sufficient size to cause delayed wound healing, or wound infection or surgical site bleeding that was unexpected and prolonged or caused haemodynamic instability (as defined by the study) that was associated with a 20 g/L drop in haemoglobin (Hb);
  - bleeding that required two or more units of wholeblood/red cells within 24 hours of the bleeding;
  - bleeding defined by the study with no further details.

Secondary outcomes

- Number of participants with minor procedure-related bleeding within seven days of surgery (e.g. haematoma, prolonged bleeding at surgical site that did not fulfil the definition for major bleeding).

- Number of platelet transfusions per participant and number of platelet components per participant.
- Number of red cell transfusions per participant and number of red cell components per participant.
- Proportion of participants requiring additional interventions to stop bleeding (surgical; medical, e.g. tranexamic acid; other blood products, e.g. fresh frozen plasma (FFP), cryoprecipitate, fibrinogen) within seven days of surgery.
- Quality of life assessment using validated tools.
- Serious adverse events due to:
  - transfusion (transfusion reactions, TRALI, transfusion-related infection, transfusion-associated circulatory overload, transfusion-related dyspnoea) within 24 hours of the transfusion;
  - surgery (e.g. delayed wound healing, infection) within 30 days after the operation.
- Length of hospital stay and length of ICU stay.
- Venous and arterial thromboembolism (including deep vein thrombosis, pulmonary embolism, stroke, myocardial infarction).

Recherche/Suchzeitraum:

- 11/2017

Qualitätsbewertung der Studien:

- Cochrane 'Risk of bias' tool

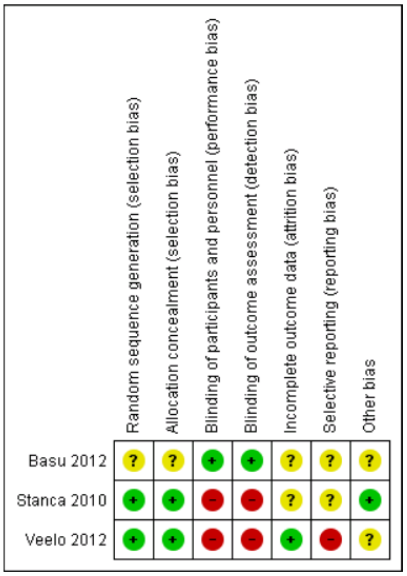
Ergebnisse

Anzahl eingeschlossener Studien:

- 3 RCTs

Qualität der Studien:

- All three included trials in this review were RCTs; however, none of the trials were free from methodological bias. See the visual summary of the risk of bias assessment on each domain. Two trials were at risk of performance and detection bias, this was due to the nature of the intervention "platelet transfusion" (Stanca 2010; Veelo 2012). Most 'Risk of bias' tool domains of one of the included trial were at unclear risk of bias as the trial was only available as an abstract (Basu 2012).



Studienergebnisse:

- Siehe auch summary of findings im Anhang

Primary outcomes:

- All-cause mortality within 30 days of the surgery
  - no evidence of a difference in the risk of death due to any cause between participants having their coagulopathy corrected (platelets, plasma, or both) and participants who did not (1 trial, 72 participants; RR 0.78, 95% CI 0.41 to 1.45; very-low quality evidence).
- Mortality secondary to bleeding; mortality secondary to thromboembolism and mortality secondary to infection (within 30 days of surgery)
  - The trial did not report these outcomes.
- All-cause mortality; mortality secondary to bleeding; mortality secondary to thromboembolism and mortality secondary to infection (within 90 days of the surgery)
  - The trial did not report these outcomes.
- Number of participants with major procedure-related bleeding within seven days of surgery
  - Veelo 2012 defined major bleeding as the presence of blood in the airways requiring repeated suction post procedure, emergency surgery, transfusion of packed red cells, or a combination of these.
  - no evidence of a difference on the incidence of procedure-related bleeding between participants having their coagulopathy corrected (platelets,plasma, or both) and participants who did not (1 trial, 72 participants; RR 1.60, 95% CI 0.29 to 8.92; very-low quality evidence).

Secondary outcomes:

- Number of participants with minor procedure-related bleeding within seven days of surgery
  - Veelo 2012 defined minor bleeding as blood loss less than 100 g that could be controlled with the application of local pressure and did not require re-exploration or transfusion of packed red cells.

  - no evidence of a difference in the risk of minor bleeding during or for 12 hours after the procedure for participants having their coagulopathy corrected (platelets, plasma, or both) and participants who did not (1 trial, 64 participants; RR 1.29, 95% CI 0.90 to 1.85).
- Number of platelet transfusions per participant and number of platelet components per participant
  - Twenty-three participants received a platelet transfusion (five buffy coat units) prior to the procedure in the intervention arm and no participants received a platelet transfusion in the comparator arm.
  - not enough evidence to help guide the use of platelet transfusions prior to surgery in people with a low platelet count.
  - no evidence for infants and children or prior to a major operation.

- Quality of the evidence
  - Overall, the quality of evidence was rated according to the GRADE methodology as very low across difference outcomes due to high risk of bias (unblinded studies); imprecision of the estimates, and indirectness (only adults with liver disease or adults in the ICU were included in the studies).

  We assessed the GRADE quality of evidence as very low for:
  - all-cause mortality;
  - number of participants with major procedure-related
  - bleeding within seven days of surgery
  - number of participants with minor procedure-related bleeding within seven days of surgery
  - serious adverse events

Anmerkung/Fazit der Autoren

Findings of this review were based on three small trials involving minor surgery in adults with thrombocytopenia. We found insufficient evidence to recommend the administration of preprocedure prophylactic platelet transfusions in this situation with a lack of evidence that transfusion resulted in a reduction in postoperative bleeding or all-cause mortality. The small number of trials meeting the inclusion criteria and the limitation in reported outcomes across the trials precluded meta-analysis for most outcomes. Further adequately powered trials, in people of all ages, of prophylactic platelet transfusions compared with no transfusion, other alternative treatments, and considering different platelet thresholds prior to planned and emergency surgical procedures are required. Future trials should include major surgery and report on bleeding, adverse effects, mortality (as a long-term outcome) after surgery, duration of hospital stay and quality of life measures.

3.3 Systematische Reviews

Es konnten keine SR im vorliegenden AWG identifiziert werden.

3.4 Leitlinien

European Association for the Study of the Liver, 2018 [2].

EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis

Leitlinienorganisation/Fragestellung

The following Clinical Practice Guidelines (CPGs) represent the first CPGs on the management of decompensated cirrhosis.

Methodik

Grundlage der Leitlinie:

A panel of hepatologists with a great interest in decompensated cirrhosis, approved by the EASL Governing Board, wrote and discussed this CPG between March 2017 and February 2018. The guidelines were independently peer reviewed, and all contributors to the CPG disclosed their conflicts of interest by means of a disclosure form provided by the EASL Office prior to work commencing. The EASL Ethics Committee reviewed the composition of the panel to eliminate the potential for real or perceived bias. The CPG panel conflict of interests are declared in this submission. These guidelines have been produced using evidence from PubMed and Cochrane database searches before 27 March 2018.

Recherche/Suchzeitraum:

- 03/2018

LoE

- I: Randomised, controlled trials
- II-1: Controlled trials without randomisation
- II-2: Cohort and case-control analytical studies
- II-3: Multiple time series, dramatic uncontrolled experiments
- III: Opinions of respected authorities, descriptive epidemiology

GoR

- 1: Strong recommendation: Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes, and cost
- 2: Weaker recommendation: Variability in preferences and values, or more uncertainty: more likely a weak recommendation is warranted. Recommendation is made with less certainty: higher cost or resource consumption

Sonstige methodische Hinweise

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Empfehlungen

- Recommendations regarding management of coagulopathy and thrombocytopenia cannot be made based on currently available data.

Referenzen aus Leitlinien
[168] De Franchis RBaveno VI faculty. Expanding consensus in portal hypertension: report of the BAVENO VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol 2015;63:743–752.
[169] Garcia-Tsao G, Sanyal AJ, Grace ND, Carey WPractice Guidelines Committee of the American Association for the Study of Liver DiseasesPractice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology 2007;46:922–938.
[199] Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology 2017;65:310–335.

NICE, 2015 [3].

National Institute for Health and Care Excellence

Blood transfusion NG 24

Leitlinienorganisation/Fragestellung

This guideline covers the assessment for and management of blood transfusions in adults, young people and children over 1 year old. It covers the general principles of blood transfusion, but does not make recommendations relating to specific conditions.

Methodik

Grundlage der Leitlinie:

A multidisciplinary Guideline Development Group (GDG) comprising health professionals and researchers as well as lay members developed this guideline. Review questions were developed in a PICO framework (patient, intervention, comparison and outcome) for intervention reviews and in a framework of setting, population, interventions, context and evaluation for qualitative reviews.

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

11. A quality rating was assigned, based on the study design. RCTs start as High, observational studies as Low, and uncontrolled case series as Low or Very low.

12. The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed below. Evidence from observational studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose–response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have ‘serious’ or ‘very serious’ risk of bias was rated down by 1 or 2 points respectively.

13. The downgraded or upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if 1, 2 or 3 points were deducted respectively.

14. The reasons or criteria used for downgrading were specified in the footnotes.

Recherche/Suchzeitraum:

- Primary search 2012
- all searches were updated on 01/2015

LoE/GoR:

- The quality is then summarised by individual study and, if using the GRADE approach, by outcome across all relevant studies.
- Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by outcome and encompass the following key features of the evidence:
  - the number of studies and the number of participants for a particular outcome
  - a brief description of the participants
  - an indication of the direction of effect (if one treatment is beneficial or harmful compared to the other, or whether there is no difference between the 2 tested treatments)
  - a description of the overall quality of evidence (GRADE overall quality).

Sonstige methodische Hinweise

/

Empfehlungen

Platelet: Thresholds and Targets

Empfehlung 1: Patients with thrombocytopenia who are bleeding

- 19. Offer platelet transfusions to patients with thrombocytopenia who have clinically significant bleeding (World Health Organization [WHO] grade 2) and a platelet count below 30×10^9 per litre. 20.
- 20. Use higher platelet thresholds (up to a maximum of 100×10^9 per litre) for patients with thrombocytopenia and either of the following:
  - severe bleeding (WHO grades 3 and 4)
  - bleeding in critical sites, such as the central nervous system (including eyes).

Quality of evidence

- No studies were identified which met the review protocol criteria.
- The recommendations for platelet transfusion for patients who were bleeding and were thrombocytopenic were based on the consensus expert opinion of the GDG members.
- There was no specific evidence available for the use of platelets in the paediatric population.

Empfehlung 2: Patients who are not bleeding or having invasive procedures or surgery

- 21. Offer prophylactic platelet transfusions to patients with a platelet count below 10×10^9 Per litre who are not bleeding or having invasive procedures or surgery, and who do not have any of the following conditions:
  - chronic bone marrow failure
  - autoimmune thrombocytopenia
  - heparin - induced thrombocytopenia
  - thrombotic thrombocytopenic purpura

Quality of evidence

- The quality of evidence for most of the outcomes was low or very low by GRADE criteria. This was largely due to risk of bias arising from a lack of allocation concealment, inadequate blinding, serious or very serious imprecision and indirectness of population and outcomes.
- The recommendation was based on this evidence and the consensus expert opinion of the GDG members.
- There was no specific evidence available for the use of platelets in the paediatric population.

Empfehlung 3: Patients who are having invasive procedures or surgery

- 22. Consider prophylactic platelet transfusions to raise the platelet count above $50x10^9$ Per litre in patients who are having invasive procedures or surgery.
- 23. Consider a higher threshold (for example 50 – 75×10^9 per litre) for patients with a high risk of bleeding who are having invasive procedures or surgery, after taking into account:
  - the specific procedure the patient is having
  - the cause of the thrombocytopenia
  - whether the patient's platelet count is falling
  - any coexisting causes of abnormal haemostasis.
- 24. Consider prophylactic platelet transfusions to raise the platelet count above 100×10^9 per litre in patients having surgery in critical sites, such as the central nervous system (including the posterior segment of the eyes).

Quality of evidence

- The recommendations for prophylactic platelet transfusions in patients who were undergoing invasive procedures or surgery were based on indirect evidence and the consensus expert opinion of the GDG members.
- The quality of the indirect evidence for most of the outcomes was low or very low by GRADE criteria. This was largely due to risk of bias arising from a lack of allocation concealment, inadequate blinding, serious or very serious imprecision and indirectness of population and outcomes.

Empfehlung 4: When prophylactic platelet transfusions are not indicated

- 25. Do not routinely offer prophylactic platelet transfusions to patients with any of the following:
  - chronic bone marrow failure
  - autoimmune thrombocytopenia

  - heparin - induced thrombocytopenia
  - thrombotic thrombocytopenic purpura.

- 26. Do not offer prophylactic platelet transfusions to patients having procedures with a low risk of bleeding, such as adults having central venous cannulation or any patients having bone marrow aspiration and trephine biopsy.

Quality of evidence

- No studies were identified which met the review protocol criteria The recommendation was based on the consensus expert opinion of the GDG members.

3.5 Ergänzende Dokumente anderer Organisationen zu möglichen Komparatoren

Es konnten keine ergänzenden Dokumente anderer Organisationen identifiziert werden.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 9 of 12, September 2018) am 18.09.2018

#	Suchfrage
1	MeSH descriptor: [Thrombocytopenia] explode all trees
2	(thrombocytopeni* OR thrombocytopaeni* OR thrombopeni*):ti,ab,kw (Word variations have been searched)
3	#1 or #2
4	#1 or #2 with Cochrane Library publication date from Sep 2013 to Sep 2018

Systematic Reviews in Medline (PubMed) am 12.09.2018

#	Suchfrage
1	thrombocytopenia[MeSH Terms]
2	((thrombocytopeni*[Title/Abstract]) OR thrombocytopaeni*[Title/Abstract]) OR thrombopeni*[Title/Abstract]
3	(#1 OR #2)
4	(((Meta-Analysis[ptyp] OR systematic[sb] OR Technical Report[ptyp])) OR (((((trials[Title/Abstract] OR studies[Title/Abstract] OR database*[Title/Abstract] OR literature[Title/Abstract] OR publication*[Title/Abstract] OR Medline[Title/Abstract] OR Embase[Title/Abstract] OR Cochrane[Title/Abstract] OR Pubmed[Title/Abstract])) AND systematic*[Title/Abstract] AND (search*[Title/Abstract] OR research*[Title/Abstract]))) OR ((((((((((HTA[Title/Abstract]) OR technology assessment*[Title/Abstract]) OR technology report*[Title/Abstract]) OR (systematic*[Title/Abstract] AND review*[Title/Abstract])) OR (systematic*[Title/Abstract] AND overview*[Title/Abstract])) OR meta-analy*[Title/Abstract]) OR (meta[Title/Abstract] AND analyz*[Title/Abstract])) OR (meta[Title/Abstract] AND analys*[Title/Abstract])) OR (meta[Title/Abstract] AND analyt*[Title/Abstract]))) OR (((review*[Title/Abstract]) OR overview*[Title/Abstract]) AND ((evidence[Title/Abstract]) AND based[Title/Abstract]))))
5	(#3 AND #4)
6	(#5) AND ("2013/09/01"[PDAT] : "3000"[PDAT])
7	(#6) NOT "The Cochrane database of systematic reviews"[Journal]
8	(#7) NOT retracted publication[ptyp]

Leitlinien in Medline (PubMed) am 12.09.2018

#	Suchfrage
1	thrombocytopenia[MeSH Terms]
2	((thrombocytopeni*[Title/Abstract]) OR thrombocytopaeni*[Title/Abstract]) OR thrombopeni*[Title/Abstract]
3	"liver diseases/surgery"[MeSH Terms]
4	(((((liver[Title/Abstract]) OR cirrhos*[Title/Abstract]) OR cirrhotic[Title/Abstract]) OR hepatitis[Title/Abstract]) OR hcv[Title/Abstract]) OR hepatocellular[Title/Abstract]

5	(((((((((surgery[Title/Abstract]) OR surgical[Title/Abstract]) OR procedure*[Title/Abstract]) OR presurgical*[Title/Abstract]) OR preoperativ*[Title/Abstract]) OR preprocedur*[Title/Abstract]) OR platelet*[Title/Abstract]) OR thrombopoietin[Title/Abstract]) OR thrombopoies*[Title/Abstract]) OR thrombopoietic[Title/Abstract]
6	(#4 AND #5)
7	platelet transfusion[MeSH Terms]
8	(platelet[Title/Abstract]) AND transfus*[Title/Abstract]
9	(#1 OR #2 OR #3 OR #6 OR #7 OR #8)
10	(((((Guideline[Publication Type]) OR Practice Guideline[Publication Type]) OR Consensus Development Conference[Publication Type]) OR Consensus Development Conference, NIH[Publication Type]) OR guideline*[Title]) OR recommendation*[Title]
11	(#9 AND #10)
12	(#11) AND ("2013/09/01"[PDAT] : "3000"[PDAT])
13	(#12) NOT retracted publication[ptyp]

Referenzen

1. **Estcourt L, Malouf R, Doree C, Trivella M, Hopewell S, Birchall J.** Prophylactic platelet transfusions prior to surgery for people with a low platelet count. Cochrane Database of Systematic Reviews [online]. 2018(9):Cd012779. URL: http://dx.doi.org/10.1002/14651858.CD012779.pub2.
2. **European Association for the Study of the Liver.** EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018;69(2):406-460.
3. **National Clinical Guideline Centre.** Blood transfusion [online]. London (GBR): National Institute for Health and Care Excellence; 2015. [Zugriff: 05.09.2018]. (NICE Guideline; Band 24). URL: https://www.nice.org.uk/guidance/ng24/evidence/full-guidance-pdf-2177160733.

Anhang

Estcourt LJ et al., 2018 [1].

Prophylactic platelet transfusions prior to surgery for people with a low platelet count

Abbildung 1: Summary of findings for the main comparison

Prophylactic platelet transfusion prior to surgery versus no prophylactic platelet transfusion prior to surgery

Patient or population: people with a low platelet count
Setting: surgery
Intervention: platelet transfusion
Comparison: no platelet transfusion

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with no platelet transfusion	Risk with platelet transfusion				
All-cause mortality within 30 days of surgery	Study population		**RR 0.78** (0.41 to 1.45)	72 (1 RCT)	⊕◯◯◯ **Very low**[a,b]	-
	405 per 1000	316 per 1000 (166 to 588)				
Mortality secondary to bleeding within 30 days of surgery - not reported	-	-	-	-	-	-
Mortality secondary to thromboembolism within 30 days of surgery - not reported	-	-	-	-	-	-
Mortality secondary to infection within 30 days of surgery - not reported	-	-	-	-	-	-
Number of participants with major bleeding within 7 days of surgery (surgical site bleeding requiring a second intervention or reoperation or surgical site bleeding that causes a haematoma or haemarthrosis of sufficient size to delay mobilisation or wound healing)	Study population		**RR 1.60** (0.29 to 8.92)	64 (1 RCT)	⊕◯◯◯ **Very low**[b,c]	-
	61 per 1000	97 per 1000 (18 to 541)				
The number of participants with minor procedure-related bleeding within 7 days of surgery	Study population		**RR 1.29** (0.90 to 1.85)	64 (1 RCT)	⊕◯◯◯ **Very low**[a,c,d]	-
	576 per 1000	743 per 1000 (518 to 1000)				
Serious adverse events (surgery-related adverse effects within 30 days)	No events occurred in either study arm			64 (1 RCT)	⊕◯◯◯ **Very low**[a,c,d]	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RCT:** randomised controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence
High quality: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a] Only adults in the intensive care unit were included in this trial (downgraded one level for indirectness).
[b] The conf idence intervals included a serious risk of harm or benef it (downgraded two levels for imprecision).
[c] This is a subjective outcome and the trial was unblinded (downgraded one level for risk of bias).
[d] The confidence intervals included a risk of harm or benefit (downgraded one level for imprecision).