Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

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

Vorgang: Tafamidis

Stand: April 2019

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

2019-B-031
Tafamidis zur Behandlung der Transthyretin-Amyloidose bei erwachsenen Patienten mit Wildtyp oder hereditärer Kardiomyopathie

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.	• Lebertransplantation • Herztransplantation
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	keine
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:	
Tafamidis-Meglumin N07XX08 Vyndaqel®	Vyndaqel ist indiziert zur Behandlung der Wildtyp- oder hereditären Transthyretin-Amyloidose bei erwachsenen Patienten mit Kardiomyopathie (ATTR-CM).
Im Anwendungsgebiet zugelassene Arzneimittel	
keine	

Quellen: AMIS-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

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

Vorgang: Tafamidis

Auftrag von:	Abt. AM
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Datum:	14. März 2019

Inhaltsverzeichnis

Abkürzungsverzeichnis

AE	Adverse events
AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
BMT	bone marrow transplantation
CR	Complete Response
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
hATTR	hereditary transthyretin-mediated amyloidosis
HDM-ASCT	high-dose melphalan/autologous transplantation
HR	Hazard Ratio
IMiDs	immunomodulatory drugs
KI	Konfidenzintervall
LoE	Level of Evidence
mBMI	modified body mass index
n.s.	Nicht signifikant
NICE	National Institute for Health and Care Excellence
NIS-LL	Neuropathy Impairment Score–Lower Limbs
Norfolk QoL-DN	Norfolk Quality of Life-Diabetic Neuropathy
OR	Odds Ratio
ORR	overall response rate
OS	Overall Survival
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
TTR	Transthyretin
TTR-FAP	Transthyretin Familial Amyloid Polyneuropathy
WHO	World Health Organization

1 Indikation

zur Behandlung der Transthyretin-Amyloidose bei erwachsenen Patienten mit Wildtyp oder hereditären Kardiomyopathie, um die Mortalität sowie die kardiovaskulär bedingte Hospitalisierung zu reduzieren.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation Transthyretin-Amyloidose durchgeführt. Der Suchzeitraum wurde auf die letzten 5 Jahre eingeschränkt und die Recherche am 20.02.2019 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 89 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 5 Quellen, die in die synoptische Evidenz-Übersicht aufgenommen wurden.

3 Ergebnisse

3.1 IQWiG-Berichte/G-BA-Beschlüsse

G-BA, 2012 [2].

Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie (AM-RL): Anlage XII - Beschlüsse über die Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V – Tafamidis Meglumin.

Anwendungsgebiet

Vyndaqel® ist indiziert zur Behandlung der Transthyretin-Amyloidose bei erwachsenen Patienten mit symptomatischer Polyneuropathie im Stadium 1, um die Einschränkung der peripheren neurologischen Funktionsfähigkeit zu verzögern.

Zweckmäßige Vergleichstherapie:

Tafamidis Meglumin ist zugelassen als Arzneimittel zur Behandlung eines seltenen Leidens nach der Verordnung (EG) Nr. 141/ 2000 des Europäischen Parlaments und des Rates vom 16. Dezember 1999 über Arzneimittel für seltene Leiden. Gemäß § 35a Absatz 1 Satz 10 gilt der medizinische Zusatznutzen durch die Zulassung als belegt.

Der Gemeinsame Bundesausschuss (G-BA) bestimmt gemäß 5. Kapitel § 12 Absatz 1 Nummer 1 Satz 2 der Verfahrensordnung des G-BA (VerfO) das Ausmaß des Zusatznutzens für die Anzahl der Patienten und Patientengruppen, für die ein therapeutisch bedeutsamer Zusatznutzen besteht. Diese Quantifizierung des Zusatznutzens erfolgt am Maßstab der im 5. Kapitel § 5 Absatz 7 Nummer 1 bis 4 VerfO festgelegten Kriterien.

Fazit / Ausmaß des Zusatznutzens / Ergebnis

geringer Zusatznutzen

3.2 Cochrane Reviews

Es wurden keine relevanten Cochrane Reviews identifiziert.

3.3 Systematische Reviews

Zhao Y et al., 2019 [5].

Tafamidis, a Noninvasive Therapy for Delaying Transthyretin Familial Amyloid Polyneuropathy: Systematic Review and Meta-Analysis.

Fragestellung

to evaluate the efficacy and safety of tafamidis in TTR-FAP patients, with the aim of improving the medical-evidence base for applying it as a treatment option for TTP-FAP.

Methodik

Population: patients diagnosed with TTR-FAP

Intervention:

- tafamidis

Komparator:

- placebo

Endpunkte:

- Neuropathy Impairment Score–Lower Limbs (NIS-LL), Norfolk Quality of Life-Diabetic Neuropathy total quality of life (TQOL) score, modified body mass index (mBMI)

Recherche/Suchzeitraum:

- A systematic search of the English-language literature in MEDLINE, PubMed, EMBASE, Web of Science, and Cochrane Library was performed through to May 31, 2018

Qualitätsbewertung der Studien:

- modified Jadad quality scoring scale

Ergebnisse

Anzahl eingeschlossener Studien:

- six studies

Qualität der Studien:

All six included studies employed randomization, concealment of allocation, and double blinding, and all of them had a Jadad score of 6 points, indicating that they were of high quality (Table 2).

Table 2. Jadad scores for the included studies

Reference (year)	Randomization	Concealment of allocation	Double blinding	Withdrawals and dropouts	Jadad score
Barroso et al., 2017[31]	2	1	2	1	6
Coelho et al., 2013[30]	2	1	2	1	6
Suhr et al., 2014[29]	2	1	2	1	6
Keohane et al., 2017[27]	2	1	2	1	6
Gundapaneni et al., 2018[28]	2	1	2	1	6
Coelho et al., 2012[32]	2	1	2	1	6

Studienergebnisse:

- The tafamidis group showed smaller changes from baseline in the Neuropathy Impairment Score–Lower Limbs [mean difference (MD)=-3.01, 95% confidence interval (CI)=-3.26 to -2.75, p<0.001] and the Norfolk Quality of Life-Diabetic Neuropathy total quality of life score (MD=-6.67, 95% CI=-9.70 to -3.64, p<0.001), and a higher modified body mass index (MD=72.45, 95% CI=69.41 to 75.49, p<0.001), with no significant difference in total adverse events
- The incidence of adverse events did not differ between tafamidis and placebo treatment except for fatigue (OR=0.13, 95% CI=0.02 to 0.72, p=0.02) and hypesthesia (OR=0.16, 95% CI=0.03 to 0.92, p=0.04).

Anmerkung/Fazit der Autoren

In conclusion, this systematic review and meta-analysis of six RCTs has demonstrated that tafamidis exhibits a slower neurologic disease progression and better preservation of nutritional status and quality of life.

The rate of adverse events did not differ between the patients in the tafamidis and placebo groups. These findings indicate that tafamidis might be a safer noninvasive option for patients with TTR-FAP.

Planté-Bordeneuve V et al., 2019 [3].

An indirect treatment comparison of the efficacy of patisiran and tafamidis for the treatment of hereditary transthyretin-mediated amyloidosis with polyneuropathy

Fragestellung

to conduct an indirect, quantitative comparison of the efficacy of patisiran and tafamidis in patients with hATTR amyloidosis with polyneuropathy using currently available data.

Methodik

Population:

- patients with hATTR amyloidosis with polyneuropathy.

Intervention:

- tafamidis

Komparator:

- a common comparator (i.e. placebo in this indirect analysis)

Endpunkte:

- mean change in NIS-LL, NIS-LL response, mean change in Norfolk QoL-DN, and mean change in mBMI

Recherche/Suchzeitraum:

- MEDLINE, Embase, the Cochrane Library, and EconLit. Keine Angabe zum Suchzeitraum.

Ergebnisse

Anzahl eingeschlossener Studien:

- 2 Studien

Table 1. Overview of trials included in the analysis.

	APOLLO	Fx-005
Primary publication	Adams et al. [16]	Coelho et al. [9][a]
Intervention	Patisiran	Tafamidis
Comparator	Placebo	Placebo
Phase	III	II/III
Key inclusion criteria	• Age 18–85 years • *TTR* mutation • hATTR amyloidosis with sensorimotor peripheral neuropathy diagnosis • NIS 5–130 • PND score ≤IIIb • Adequate liver and renal function	• Age 18–75 years • V30M *TTR* mutation • hATTR amyloidosis with peripheral or autonomic neuropathy • Biopsy-confirmed amyloid deposits • Karnofsky performance status ≥50 • Adequate liver and renal function
Duration	18 months	18 months
Primary outcomes	Change in mNIS+7	NIS-LL response Change in Norfolk QoL-DN
Select other outcomes	Change in Norfolk QoL-DN (secondary) Change in mBMI (secondary)	Change in NIS-LL (secondary) Change in mBMI (secondary)
Key findings, LS mean difference (study drug vs. placebo)[b]	mNIS+7: −34.0 points[c] Norfolk QoL-DN: −21.1 points[c] NIS-LL: −11.2 points[c,d] mBMI: +115.7 kg/m^2 × g/dL[c]	NIS-LL response: 45.3% (tafamidis) vs. 29.5% (placebo) Norfolk QoL-DN: −5.2 points NIS-LL: −2.7 points[c] mBMI: +73.1 kg/m^2 × g/dL[c]

[a]For this analysis, NIS-LL data for the Fx-005 trial were extracted from Keohane et al. [28]; all other data were extracted from the primary publication.
[b]APOLLO results taken from the modified intent-to-treat population; Fx-005 results taken from the intent-to-treat population.
[c]$p < 0.05$.
[d]Change in NIS-LL was derived from the components of NIS+7; NIS-LL response was calculated *post hoc*.
hATTR: hereditary ATTR amyloidosis; LS: least-squares; mBMI: modified body mass index; mNIS+7: modified Neuropathy Impairment Score +7; NIS: Neuropathy Impairment Score; NIS-LL: Neuropathy Impairment Score-Lower Limbs; Norfolk QoL-DN: Norfolk Quality of Life-Diabetic Polyneuropathy; PND: polyneuropathy disability; TTR, transthyretin; V30M, valine to methionine mutation at amino acid 30.

Qualität der Studien:

- Beide Studien RCTs

Studienergebnisse:

Indirect treatment comparisons were performed using the standard pairwise Bucher method

- NIS-LL: The base-case analysis indicated that patisiran had a significantly greater treatment effect on NIS-LL compared with tafamidis (difference in mean change from baseline to Month 18 of –5.49; 95% CI: –10.01 to –0.97). This greater benefit of patisiran vs. tafamidis on NIS-LL was supported by the sensitivity analysis, with significant differences observed in the mITT subgroup (–8.50; 95% CI: –12.30 to –4.70), and the FAP Stage 1 and V30M subgroup (–7.19; 95% CI: –12.12 to –2.26), despite the small sample size. There was also a trend toward a greater treatment effect with patisiran vs. tafamidis in the Stage 1 and treatment-naïve subgroup.
- NIS-LL response: For NIS-LL response, the base-case analysis trended toward a greater treatment effect for patisiran compared with tafamidis (n.s.). This trend was supported by a significantly greater treatment effect for patisiran vs. tafamidis in the mITT subgroup (OR 4.29; 95% CI: 1.45–12.72) and FAP Stage 1 and V30M subgroup (OR 11.37; 95% CI: 1.16–

111.49). A trend toward a greater treatment effect was observed in the Stage 1 and treatment-naïve subgroup.

- Norfolk QoL-DN: Similar to the NIS-LL results, the base-case analysis indicated a significantly greater treatment effect for patisiran compared with tafamidis for the difference in mean change from baseline to Month 18 in Norfolk QoL-DN (–13.10; 95% CI: –23.55 to –2.66). In the sensitivity analysis, significantly greater treatment effects for patisiran vs. tafamidis were also observed in the mITT subgroup (–15.90; 95% CI: –24.78 to –7.02), and Stage 1 and treatment-naïve subgroup (–19.00; 95% CI: –32.82 to –5.18). A trend toward a greater treatment effect was observed in the Stage 1 and V30M subgroup.
- mBMI: For mBMI, the base-case analysis trended toward a greater treatment effect for patisiran compared with tafamidis for the difference in mean change from baseline to Month 18 (+47.40; 95% CI: –7.70 to 102.50). This was supported by the sensitivity analyses which saw similar trends in all subgroups despite small sample sizes.
- Safety: Safety outcomes were not compared as part of this ITC because of differences in definitions of adverse events (AEs) and serious AEs (SAEs) between trials.

Anmerkung/Fazit der Autoren

Overall, the results of this ITC suggest patisiran has a greater benefit compared with tafamidis in patients with FAP Stage 1 hATTR amyloidosis with polyneuropathy. This benefit was seen across all endpoints measured, with statistically significant differences observed for differences in mean change from baseline in NIS-LL and Norfolk QoL-DN. Similar results were also observed across all sensitivity analyses. Although these findings have important limitations, the consistency of the results across subgroups, which were analyzed to address these limitations, supports the validity of the ITC. This analysis provides an in-depth and quantitative comparison of the efficacy data currently available.

Kommentare zum Review

- while both trials enrolled patients with hATTR amyloidosis with polyneuropathy, there were differences in baseline characteristics, notably for mutation type, severity of polyneuropathy, and prior hATTR amyloidosis pharmacotherapy use. → therefore sensitivity analyses were conducted
- small number of patients involved in the two pivotal trials
- indirect comparisons between these two therapies could not be conducted among patients with non-V30M mutations or more advanced neuropathy stages, as these patients were not enrolled or evaluated as part of the tafamidis Fx-005 trial.

3.4 Leitlinien

Priori SG et al., 2015 [4].

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC)

Leitlinienorganisation/Fragestellung

Update to the American College of Cardiology (ACC)/American Heart Association (AHA)/ESC 2006 Guidelines for management of patients with ventricular arrhythmias (VA) and the prevention of sudden cardiac death (SCD)

Methodik

Grundlage der Leitlinie

Members of this Task Force were selected by the ESC to represent professionals involved with the medical care of patients with this pathology. Selected experts in the field undertook a comprehensive review of the published evidence for management (including diagnosis, treatment, prevention and rehabilitation) of a given condition according to ESC Committee for Practice Guidelines (CPG) policy. A critical evaluation of diagnostic and therapeutic procedures was performed, including assessment of the risk–benefit ratio. Estimates of expected health outcomes for larger populations were included, where data exist. The level of evidence and the strength of the recommendation of particular management options were weighed and graded according to predefined scales (siehe unten)

The experts of the writing and reviewing panels provided declarations of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest.

The ESC Guidelines undergo extensive review by the CPG and external experts.

The Guidelines were developed after careful consideration of the scientific and medical knowledge and the evidence available at the time of their dating.

LoE/GoR

Table 1 Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

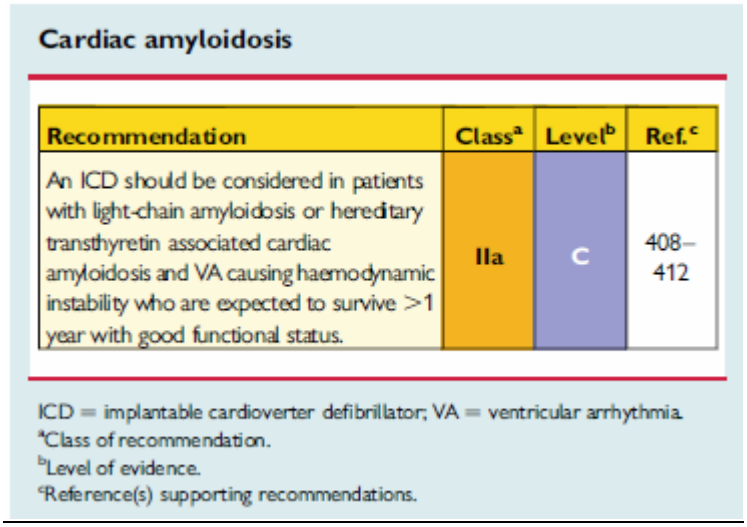
Table 2 Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Empfehlungen

7.4 Infiltrative cardiomyopathies

- 7.4.1 Cardiac amyloidosis



Cardiac amyloidosis

Recommendation	Class[a]	Level[b]	Ref.[c]
An ICD should be considered in patients with light-chain amyloidosis or hereditary transthyretin associated cardiac amyloidosis and VA causing haemodynamic instability who are expected to survive >1 year with good functional status.	IIa	C	408–412

ICD = implantable cardioverter defibrillator; VA = ventricular arrhythmia.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

- *Erläuterungen:*

  The two main types of cardiac amyloidosis are light-chain amyloidosis, caused by deposition of monoclonal light chains, and hereditary transthyretin-associated amyloidosis, in which normal (wild-type) or mutant transthyretin is deposited in the myocardium.(…)

  Based on such limited data, ICDs should be considered in patients with light-chain amyloidosis or hereditary transthyretin-associated amyloidosis that experience sustained VA and have a life expectancy >1 year. There are insufficient data to provide recommendations on primary prophylaxis.

Adams D et al., 2016 [1].

First European consensus for diagnosis, management, and treatment of transthyretin familial amyloid polyneuropathy

Zielsetzung:

This review aims to consolidate the existing literature and present an update of the best practices in the management of TTR-FAP in Europe. A summary of the methods used to achieve a TTR-FAP diagnosis is presented, as well as a review of available treatments and recommendations for treatment according to disease status.

Methodik:

This article is based on outcomes from two roundtable meetings of the European Network for TTRFAP (ATTReuNET) (November 2012 and March 2014) and a comprehensive review of the published literature. The group comprised 14 TTR-FAP experts from 10 European countries. The experts completed a semistructured questionnaire on the local practice of TTR-FAP disease management in preparation for both meetings. Groupmembers are clinicians from a variety of specialties, including neurology, internal medicine, cardiology, and nephrology. Electronic database searches (NCBI PubMed) formed the basis of the literature search within the time frame (1952 to December 2014). Key search were stated. Terms included

Sonstige methodische Hinweise

- Diese Quelle erfüllt nicht ausreichend die methodischen Anforderungen. Aufgrund limitierter höherwertiger Evidenz, wird sie jedoch ergänzend dargestellt.

Empfehlungen:

Disease management strategies for transthyretin familial amyloid polyneuropathy

The management of TTR-FAP has expanded significantly in recent years; with the availability of pharmacotherapeutic alternatives, liver transplantation is no longer the only treatment option [26]. A comprehensive care package and a multidisciplinary approach are required to manage this multisystem disease. Targeted therapy is essential in the first instance to prevent further production of amyloid deposits. Thereafter, symptomatic therapy of sensorimotor and autonomic polyneuropathy and cardiac, renal, and ocular injury is required [6, 10]. Finally, genetic counselling to patients and relatives is recommended [37].

Liver transplant

Prior to the pharmacotherapy era and as early as 1990, orthotopic liver transplant was the standard of care for patients with TTR-FAP [10,26,38]. […] Whereas liver transplant removes the main source of mutated TTR [42–44], it does not prevent progression of cardiac disease because the wild-type TTR may continue to further expand existing amyloid deposits in the heart [45, 46]. Therefore, continued scrutiny of the cardiac system is warranted, as some patients will develop atrioventricular blocks or infiltrative cardiomyopathy several years or decades later; a combined heart and liver transplant may be recommended in selected patients with non-Val30Met mutations and cardiomyopathy [47, 48, 49–51]. However, ocular and central nervous system involvements often progress and/or appear after liver transplant due to the local synthesis of mutated TTR in retinal epithelium and coroid plexus [52–54].

Tafamidis

Tafamidis is a first-in-class therapy that slows the progression of TTR amyloidogenesis by stabilizing the mutant TTR tetramer, thereby preventing its dissociation into monomers and amyloidogenic and toxic intermediates [55,56]. Tafamidis is currently indicated in Europe for the treatment of TTR amyloidosis in adult patients with stage I symptomatic polyneuropathy to delay peripheral neurological impairment [57]. […] Tafamidis is not only effective in patients exhibiting the Val30Met mutation; it also has proven efficacy, in terms of TTR stabilization, in non-Val30-Met patients over 12 months [61]. Although tafamidis has demonstrated safe use in patients with TTR-FAP, care should be exercised when prescribing to those with existing digestive problems (e.g., diarrhoea, faecal incontinence) [60].

Symptomatic management

The management of symptoms associated with sensory-motor neuropathy and autonomic dysfunction should be initiated immediately following diagnosis and should be tailored to the individual patient [10]. Symptomatic treatment may include painkillers, antidiarrhoeal drugs, treatment of symptomatic orthostatic hypotension, diuretics for patients with cardiac failure, prophylactic pacemaker implantation for severe cardiac conduction disorders [32], or vitrectomy/trabeculectomy for the treatment for ocular amyloidosis or glaucoma, respectively [10].

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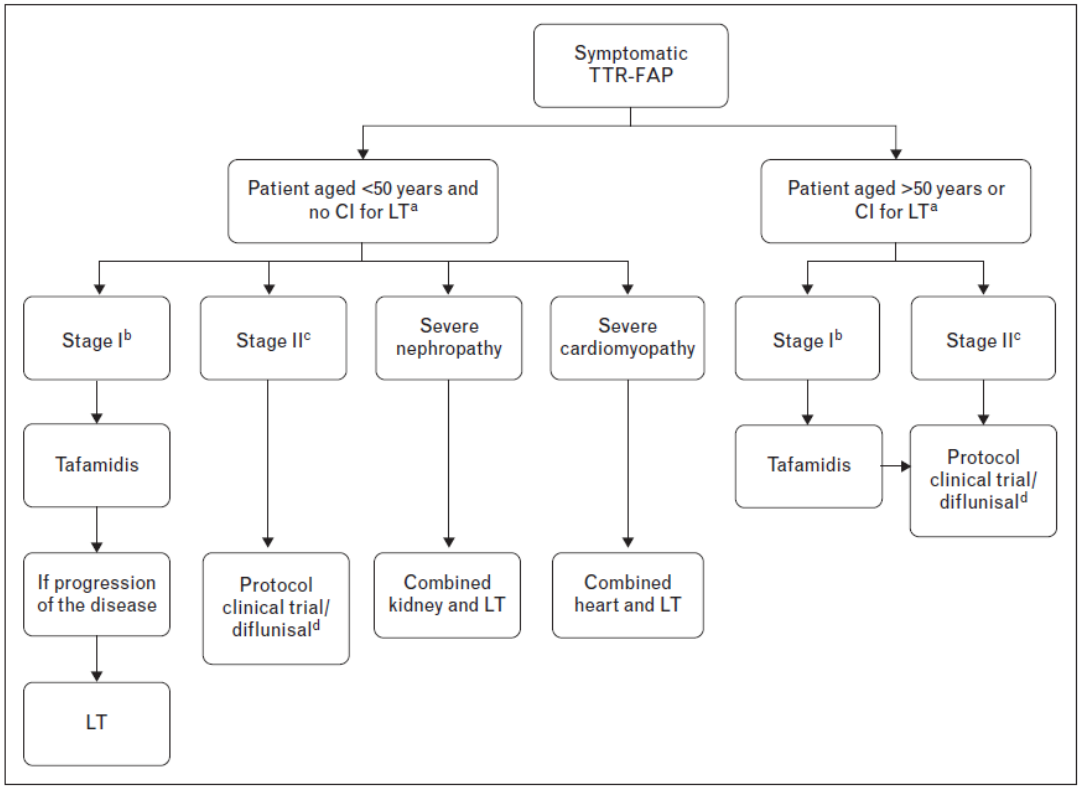

FIGURE 1. Strategy for specific therapy in TTR-FAP. CI, contraindications; LT, liver transplantation; TTR-FAP, transthyretin familial amyloid polyneuropathy. [a]CI for LT include: active and uncontrolled cancer; aged > 50 years for males and > 70 years for females [39▪▪,77], except for Italy (aged >65 years); modified body mass index below 800 kg/m^2·g/L; some non-Val30Met *TTR* mutations; cardiac insufficiency. [b]Stage I: walking unaided outside. [c]Stage II: walking with aid. [d]Protocol clinical trial for antisense oligonucleotides, small interfering RNA, combination doxycycline–tauroursodeoxycholic acid; or diflunisal off-label. Adapted from [1▪].

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library (Cochrane Database of Systematic Reviews) am 20.02.2019

#	Suchfrage
1	MeSH descriptor: [Amyloidosis] explode all trees
2	(amyloid*):ti,ab,kw (Word variations have been searched)
3	(transthyretin OR cardiac OR cardiomyopath*):ti,ab,kw (Word variations have been searched)
4	(ATTR OR ATTRwt OR wtATTR OR TTRwt OR wtTTR OR ATTRw OR ATTRm OR mATTR OR TTRm OR mTTR OR hATTR):ti,ab,kw (Word variations have been searched)
5	#1 OR (#2 AND #3) OR #4
6	#5 with Cochrane Library publication date from Feb 2014 to Feb 2019, in Cochrane Reviews

Systematic Reviews in Medline (PubMed) am 19.02.2019

#	Suchfrage
1	amyloidosis[MeSH Terms]
2	amyloid*[Title/Abstract]
3	(transthyretin[Title/Abstract] OR cardiac[Title/Abstract] OR cardiomyopath*[Title/Abstract])
4	(ATTR[Title/Abstract] OR ATTRwt[Title/Abstract] OR wtATTR[Title/Abstract] OR TTRwt[Title/Abstract] OR wtTTR[Title/Abstract] OR ATTRw[Title/Abstract] OR ATTRm[Title/Abstract] OR mATTR[Title/Abstract] OR TTRm[Title/Abstract] OR mTTR[Title/Abstract] OR hATTR[Title/Abstract])
5	(#1 OR (#2 AND #3) OR #4)
6	(#5) AND ((Meta-Analysis[ptyp] 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 systematic 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 (systematic 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 ("2014/02/01"[PDAT] : "3000"[PDAT])
8	(#7) NOT "The Cochrane database of systematic reviews"[Journal]
9	(#8) NOT retracted publication[ptyp]

Leitlinien in Medline (PubMed) am 19.02.2019

#	Suchfrage
1	amyloidosis[MeSH Terms]
2	amyloid*[Title/Abstract]
3	(transthyretin[Title/Abstract] OR cardiac[Title/Abstract] OR cardiomyopath*[Title/Abstract])
4	(ATTR[Title/Abstract] OR ATTRwt[Title/Abstract] OR wtATTR[Title/Abstract] OR TTRwt[Title/Abstract] OR wtTTR[Title/Abstract] OR ATTRw[Title/Abstract] OR ATTRm[Title/Abstract] OR mATTR[Title/Abstract] OR TTRm[Title/Abstract] OR mTTR[Title/Abstract] OR hATTR[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 ("2014/02/01"[PDAT] : "3000"[PDAT])
8	(#7) NOT retracted publication[ptyp]

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