CHALLENGES IN SELECTING RELEVANT COMPARATOR THERAPIES IN INDICATIONS WITH LOW EVIDENCE USING THE EXAMPLE OF GERMAN BENEFIT ASSESSMENTS WITH THE APPROPRIATE COMPARATOR THERAPY "TREATMENT OF PHYSICIANS CHOICE"

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OBJECTIVES

The selection of relevant comparator therapies is a major challenge in indications with low evidence. The aim of this analysis was to use the example of German benefit assessments to identify which comparator therapies are used in indications with low evidence and which influencing factors play a role in selecting these appropriate comparator therapies.

METHODS

In the German health technology assessment (HTA) system, the comparator therapies "treatment of physicians choice" (TPC) with or without best supportive care (BSC) are often selected by the Federal Joint Committee (G-BA) in indications with low evidence. In order to analyse potential influencing factors, all published benefit assessments with comparator therapies TPC were extracted and analysed for differences and similarities with regard to the choice of comparator therapies. First, all G-BA benefit assessments with the comparator therapy "treatment of physicians choice" were extracted with the IQVIA™ HTA Accelerator platform for the time period 1st January 2011 until 21st January 2022 (n = 44; Fig. 1)[1]. Second, benefit assessments of orphan drugs with a revenue below a 50 million € threshold (see box 1), diagnostics or incomplete dossiers were excluded from the assessment pool (n = 5)[1, 2]. In a third step, the extracted and cleared assessments were filtered based on the comparator therapy TPC with and without BSC (n = 7; n = 32). In the subsequent analysis step, the identified assessments in particular Module 3.1 and the assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) were analyzed in detail with regards to the rational of the choice of comparator therapy by the G-BA[1].

RESULTS

By 21st of January 2022, a total of 44 benefit assessments with the comparator therapy TPC assessed by the G-BA could be identified. 5 assessments were excluded due to diagnostics or incomplete dossiers or the legal requirements for the benefit assessment of orphan drugs by the G-BA (Fig. 1). In 7 of the 39 remaining assessments, BSC was included as comparator therapy (Fig. 2). 21 of the 39 assessments (53.8%) are related to oncology indications including 5 extracted assessments with TPC including BSC (Fig. 3). The low evidence base and the availability of several equivalent therapy options in the indication are main characteristics for benefit assessments with TPC (Tab. 1). In addition, the analysis has shown a discrepancy between therapies approved in the indication and therapies recommended in guidelines in many cases (8/32; 25,0%). BSC is included as comparator therapy with TPC if no other therapy is suitable for some of the patients (Tab. 2)[1].

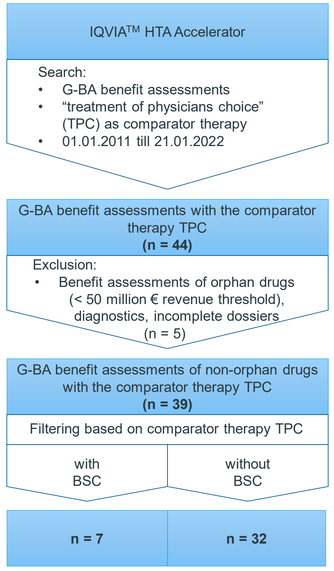

Figure 1: Flow chart of the search for relevant G-BA benefit assessments[1]

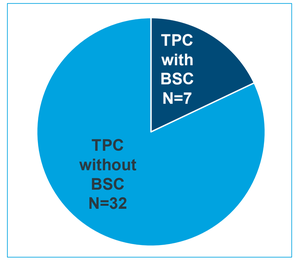

Figure 2: Share of G-BA benefit assessments with the comparator therapy TPC with and without BSC[1]

Box 1: Legal requirements for the benefit assessment of orphan drugs by the G-BA[2]

For orphan drugs, the additional benefit is considered as proven by the marketing authorization. Evidence of the additional benefit in relation to the appropriate comparator therapy must only be submitted if the revenue of the orphan drug with the statutory health insurance at pharmacy sales prices exceed an amount of 50 million euros within 12 months.

CONCLUSION

In order to identify suitable comparator therapies in indications with low evidence, HTA bodies such as the G-BA aim not to exclude any therapy option with sufficient evidence to ensure that all included patients receive the optimal comparator therapy. BSC is a viable option in cases where there is a lack of approved substances with a convincing evidence basis, often this is the case for substances with a long-standing approval and no new evidence.

References:
1. G-BA Benefit Assessment (2022).Nutzenbewertung von Arzneimitteln: Verfahren nach §35a SGB V. https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/.
2. Gemeinsamer Bundesausschuss (G-BA). Verfahrensordnung des Gemeinsamen Bundesausschusses. (Stand: 17. August 2022). 2022.

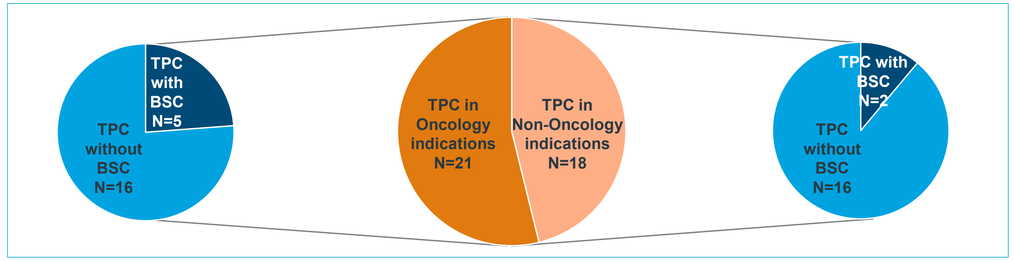

Figure 3: Share of G-BA benefit assessments in oncology and non-oncology indications with the comparator therapy TPC with and without BSC[1]

Rationale for TPC (without BSC) as comparator therapy	Number of G-BA benefit assessments with rationale included
No standard therapy	6*
Discrepancy between therapies approved in the indication and therapies recommended in guidelines	8*
No specific therapy recommendations	1
Other rationale	19

Table 1: Overview of rationale for TPC (without BSC) as comparator therapy and number of related identified G-BA benefit assessments[1] *Two assessments include two displayed rationales

Active substance and indication of G-BA benefit assessment	Submitting company	Decision date	Rationale for the inclusion of BSC in TPC
Cemiplimab (Libtayo) for the treatment of metastatic or locally advanced cutaneous squamous cell carcinoma in adults ineligible for curative surgery or radiation - original	Sanofi	06.02.2020	No rationale mentioned
Idelalisib (Zydelig) in combination with ofatumumab for the treatment of chronic lymphocytic leukemia in adult patients - extension of indication	Gilead Sciences	16.03.2017	BSC is included as a recommendation in the guidelines
Larotrectinib (Vitrakvi) for the treatment of adult and paediatric patients with solid tumours that display a NTRK gene fusion - original	Bayer	02.04.2020	No satisfactory treatment options in the indication
Nivolumab (Opdivo) as monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based combination chemotherapy - extension of indication	Bristol-Myers Squibb	01.07.2021	No rationale mentioned
Onasemnogene abeparvovec (Zolgensma) for the treatment of patients with 5q spinal muscular atrophy (SMA) - resubmission	Novartis	04.11.2021	No rationale mentioned
Risdiplam (Evrysdi) for the treatment of 5q spinal muscular atrophy (SMA) in patients aged 2 months and older with SMA Type 1, Type 2 or Type 3 or with 1 to 4 SMN2 copies - original	Roche	21.10.2021	BSC currently the only available treatment option
Venetoclax (Venclyxto) with rituximab for the treatment of chronic lymphocytic leukemia in adults after prior therapy - extension of indication	Abbvie	16.05.2019	BSC for patients who have failed previous therapies

Table 2: Overview of identified benefit assessments with the comparator therapy TPC including BSC[1]

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