Patient Individual Therapy as Appropriate Comparator in AMNOG-Dossiers in the Field of Oncology: Status Quo and Strategic Implications for Pharmaceutical Companies

Corinna Templin, PhD; Nadia Italia, MPH; Daniela Damen, PhD; Werner Kulp, PhD | Xcenda GmbH, Hannover, Germany

OBJECTIVES

- For the mandatory assessment of the benefit of new drugs in Germany, an appropriate comparator is defined by the Federal Joint Committee (FJC).
- Appropriate comparators can be categorized into four classes: (1) one specific drug; (2) a list of drugs; (3) best supportive care (BSC); and (4) patient individual therapy.
- The goal of this analysis was to determine, which methodological challenges come along with the assignment of patient individual therapy as an appropriate comparator and how this comparator impacts the outcome of the benefit assessment.

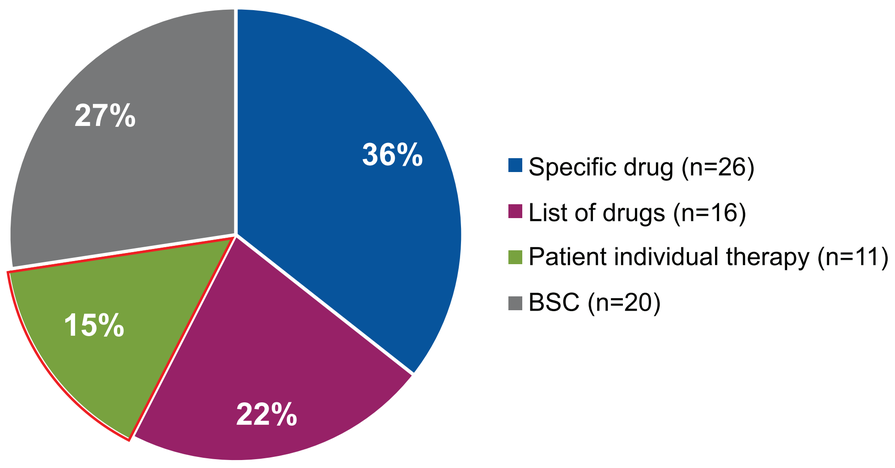
METHODS

- Information was retrieved from all non-orphan AMNOG-dossiers in the field of oncology published at the FJC website (https://www.g-ba.de) until the end of 2015.
- Information concerning indication, size of target population, line of therapy, and outcome was obtained. In addition, it was examined whether the pharmaceutical companies followed the definition of the appropriate comparator by the FJC in their dossiers or not.

RESULTS

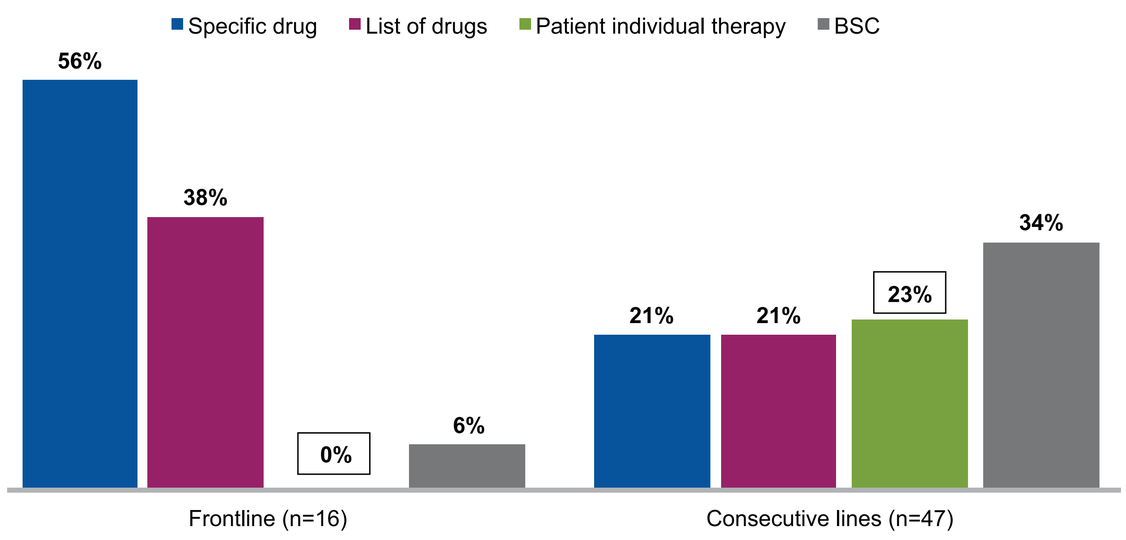
- 42 relevant AMNOG-dossiers in the field of oncology were published within the years 2011-2015 and conclusively assessed by the FJC. These dossiers included 73 separately evaluated (sub)labels.

Figure 1: Patient individual therapy is the least common appropriate comparator in oncological AMNOG-dossiers



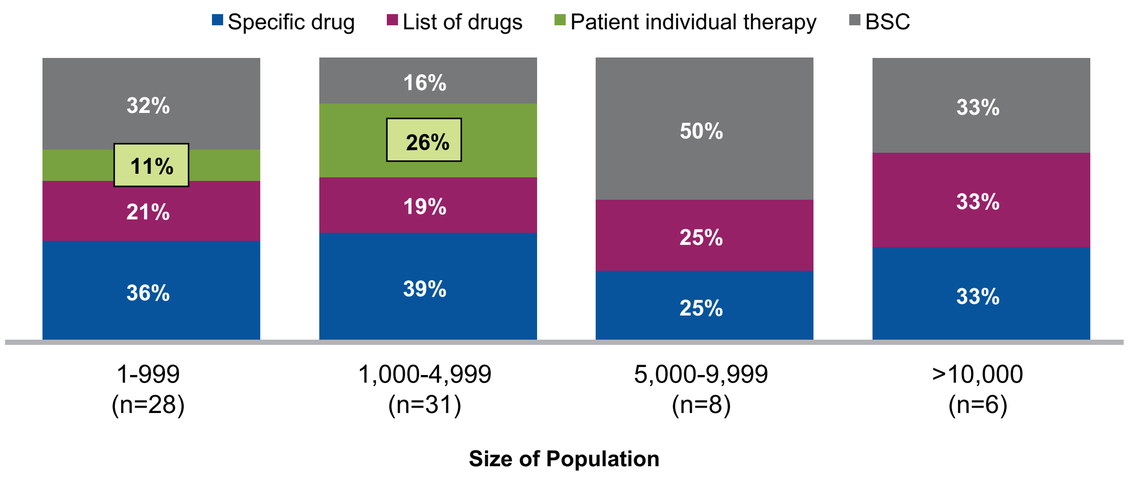
- The assignment of appropriate comparators was distributed as follows: 26 (36%) specific drug; 16 (22%) list of drugs; 20 (27%) BSC; and 11 (15%) patient individual therapy (**Figure 1**).
- Patient individual therapy was named as the appropriate comparator in 11 cases (15%) (**Figure 1**).
- The most common appropriate comparator was a specific drug (36%) (**Figure 1**).

Figure 2: In frontline therapies, patient individual therapy was not assigned as appropriate comparator



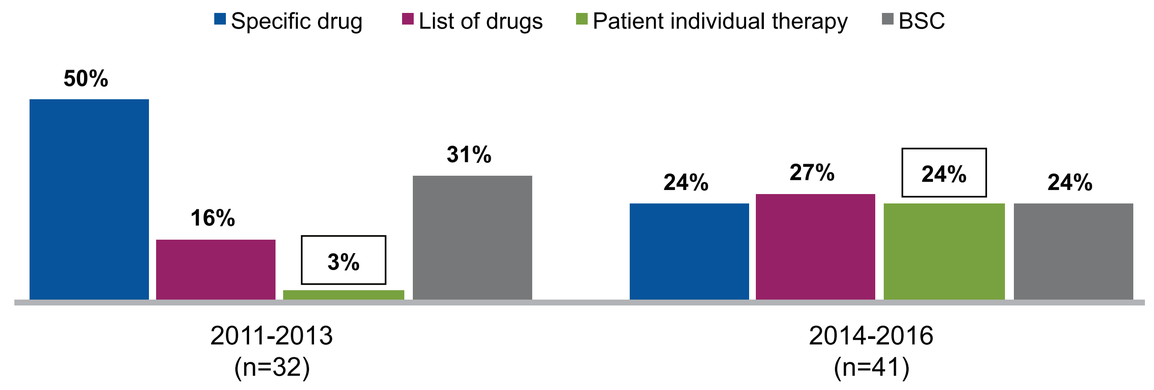
- Patient individual therapy was not assigned as the appropriate comparator for drugs designated for frontline therapies (**Figure 2**).
- BSC was the most common comparator in consecutive therapy lines (34%). The distribution of the other options was comparable (21% for specific drug and list of drugs, respectively; 23% for patient individual therapy) (**Figure 2**).

Figure 3: Patient individual therapy was assigned as appropriate comparator in small target populations only



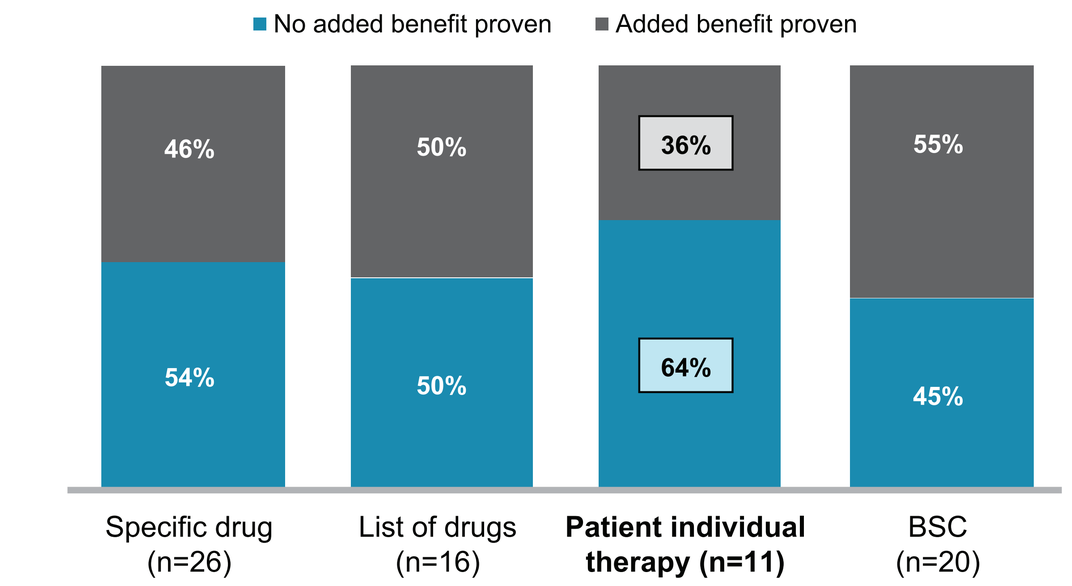
- The size of the target population seems to influence the assignment of the appropriate comparator (**Figure 3**).
- If the size of the target population exceeds 5,000 patients, patient individual therapy was not assigned as the appropriate comparator (**Figure 3**).

Figure 4: Patient individual therapy was increasingly assigned as appropriate comparator in the last three years



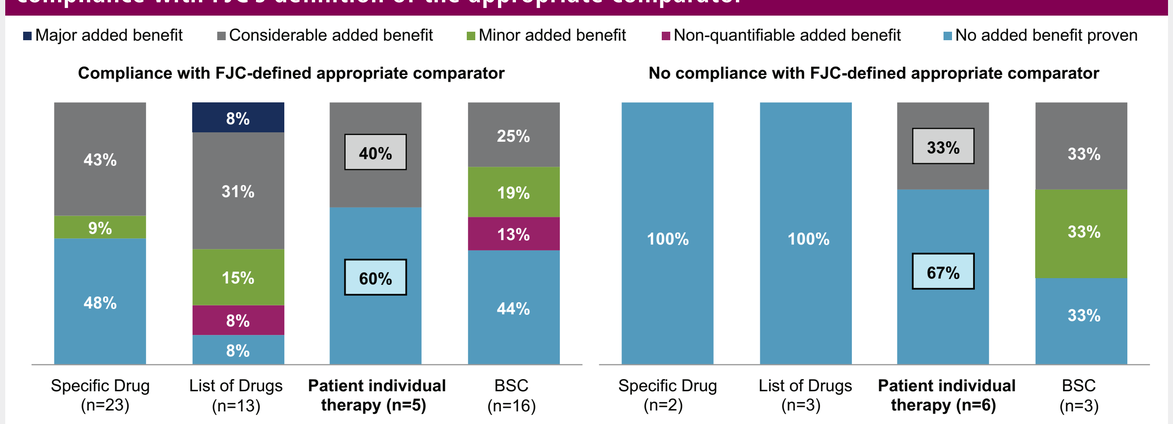
- In the first three years of AMNOG (2011-2013), a specific drug was defined as the appropriate comparator in half of all cases. Patient individual therapy was defined as the appropriate comparator in only 3% of the dossiers in that period (**Figure 4**).
- The pattern of allocation has changed in the following years (2014-2016). The increase of patient individual therapy as the appropriate comparator (3% vs. 24%) is striking (**Figure 4**).

Figure 5: Labels with patient individual therapy as appropriate comparator less often achieved an added benefit



- In the majority of cases the assessment of AMNOG-dossiers with patient individual therapy as the FJC-defined appropriate comparator resulted in no added benefit (64%). However, in four cases (36%) a considerable added benefit was proven (**Figure 5**).
- Dossiers with BSC as the appropriate comparator had the highest probability to gain an added benefit (55%) (**Figure 5**).

Figure 6: Patient individual therapy: There may be proof of an added benefit irrespective of compliance with FJC's definition of the appropriate comparator



- Only two of five dossiers that explicitly used patient individual therapy as comparator in the relevant trials achieved an added benefit (40%) (**Figure 6**).
- The specific criteria of patient individual therapy as the appropriate comparator were not met in six dossiers. However, in two cases (33%) a considerable added benefit was granted (**Figure 6**).
- In dossiers with BSC as the appropriate comparator the extent of the added medical benefit was also independent of the choice of the comparator. In this category the likelihood of achieving an added benefit was comparably high (**Figure 6**).
- On the contrary, if a specific drug or a list of drugs was defined as the appropriate comparator, an added benefit was only granted, if the company's choice of the appropriate comparator was in line with the FJC's choice (**Figure 6**).
- A major benefit was only achieved if the appropriate comparator was a list of drugs (**Figure 6**).

CONCLUSIONS

- Patient individual therapy (i.e. all relevant drugs can be used to the discretion of the study physician) is rarely used in clinical trials. Despite this, patient individual therapy seems to become more relevant as appropriate comparator, as indicated by the increasing allocation by the FJC.
- As of now, patient individual therapy is not defined as an appropriate comparator by the FJC for drugs designated for frontline therapy and if the size of the target population exceeds 5,000 patients.
- The chance of getting an added benefit granted is low, if the appropriate comparator is patient individual therapy.
- In the case of patient individual therapy and BSC, there seems to be more flexibility regarding the comparator used in the AMNOG dossier. In some cases, an added benefit was granted, although the appropriate comparator as defined by the FJC was not utilized.
- If a specific drug or a list of drugs is assigned as the appropriate comparator, an added benefit could only be achieved, if the company's choice of the comparator matched the FJC requirements.
- In order to maximize the likelihood of getting an added benefit granted, HTA specific requirements should be taken into account for study design.

Presented at ISPOR 19th Annual European Congress | 29 October-2 November 2016 Vienna, Austria PCN242