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Significant benefit of oncology products at MA: the COMP experience

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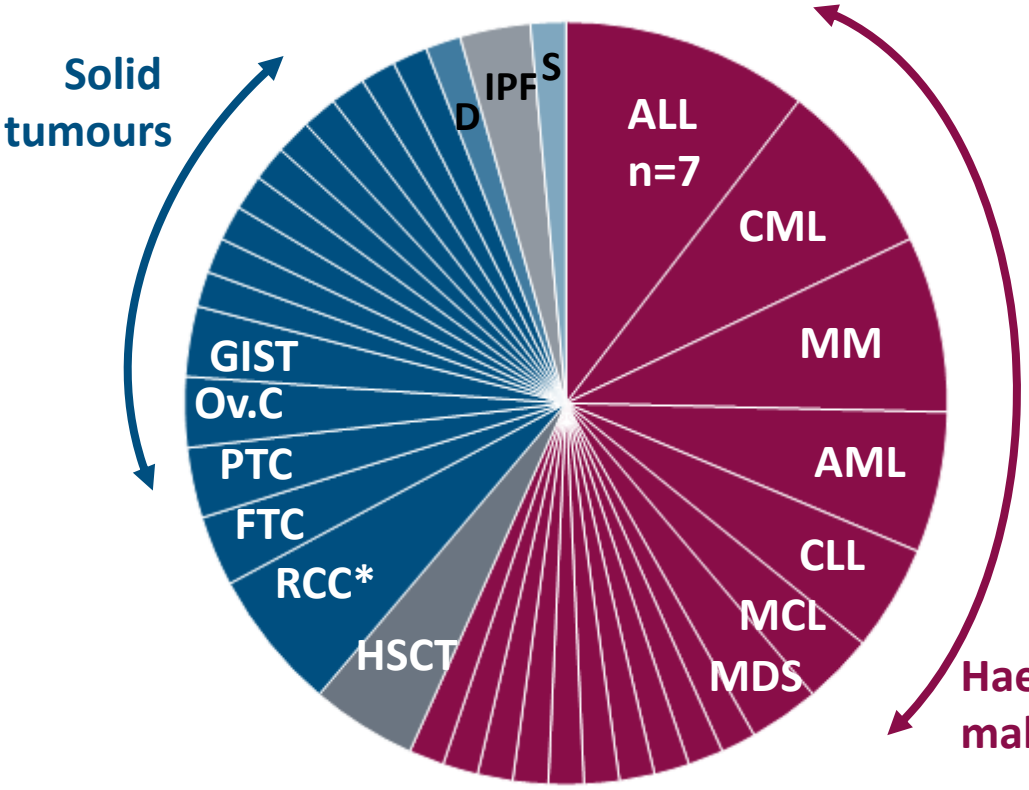
Oncology OMPs by orphan condition (2000-2015)



48 Orphan medicinal products (OMP) for **37** different conditions

n=12 OMP with >1 condition

n=14 conditions > 1 OMP

n = 67 decisions by the COMP

Listed: ≥ 2 products/condition **D**: Diagnosis **S**: Supportive treatment
IPF: Idiopathic pulmonary fibrosis **HSCT** Haematological stem cell transplantation

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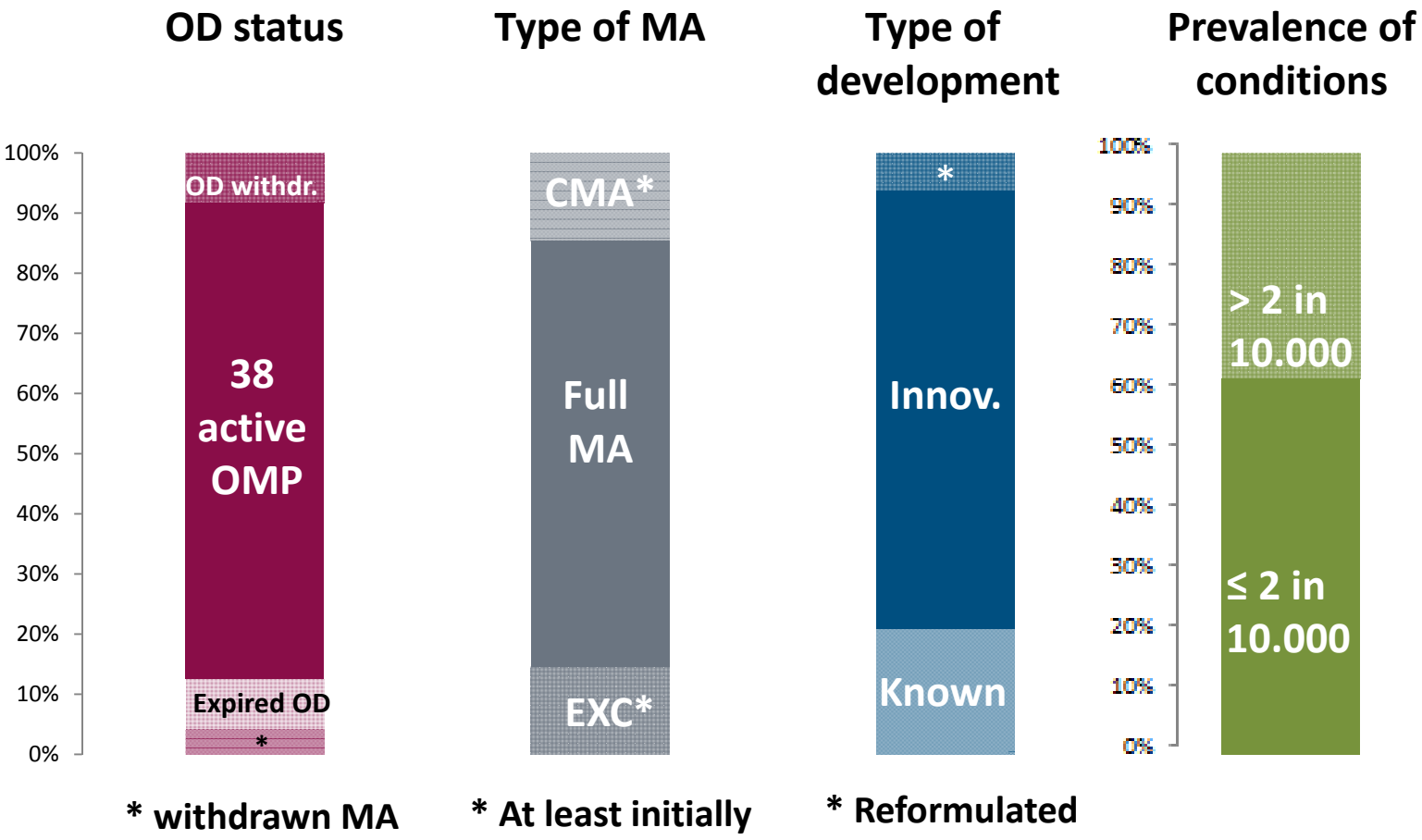
Some statistics on oncology OMPs



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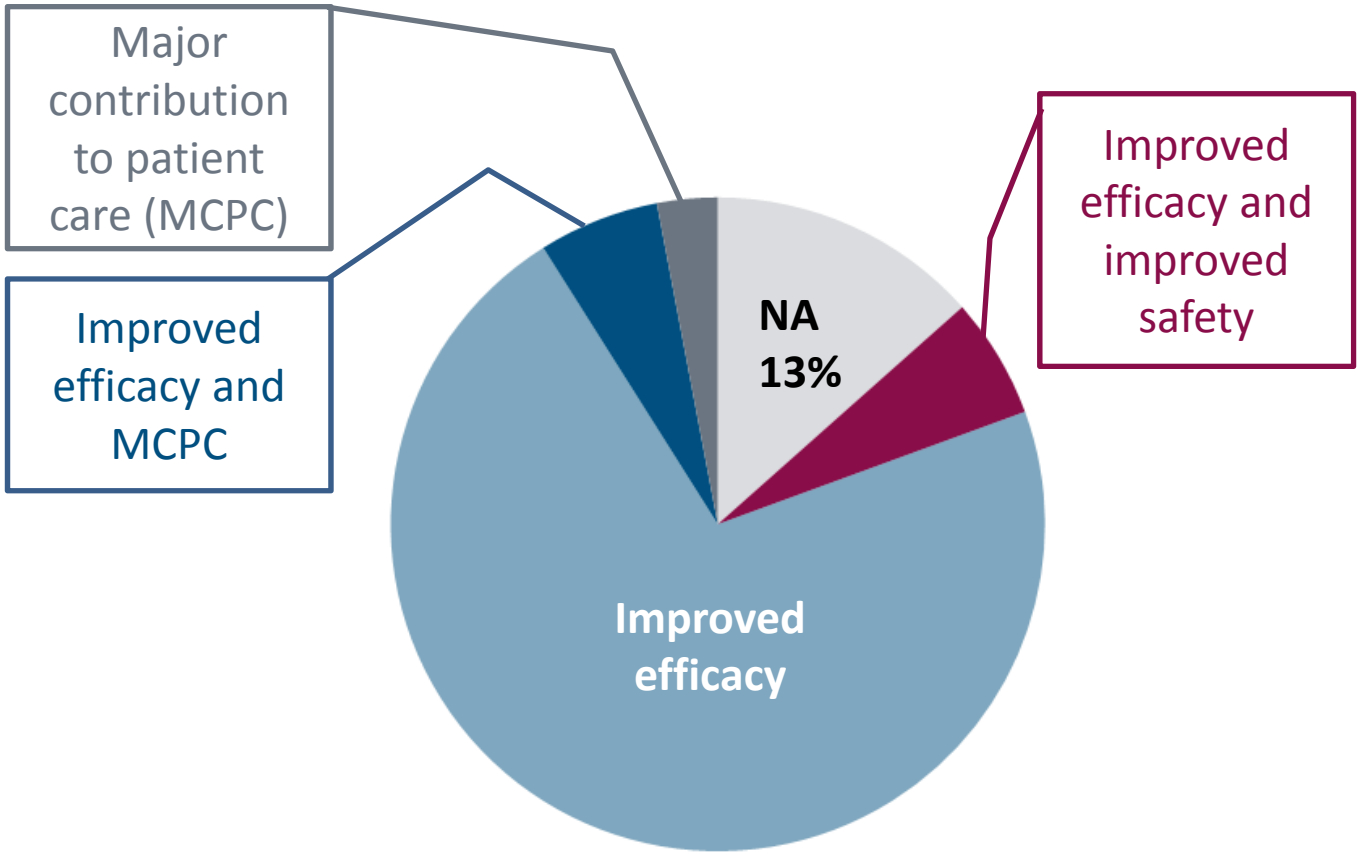
Significant benefit in oncology OMPs



⇒ Combination of categories possible/necessary!

Hypothetical orphan at review - 1

Orphan condition X - 2. line	"Satisfactory Method " (SM) 1-3	Product A - SB required!
Scientific evidence	**SM1**: SoC 1. line **SM2**: SoC 2. line **SM3**: limited efficacy, authorised beyond 2. line	**Active-controlled trial vs SM2** Primary endpoint PFS **HR=0.31** OS numerical benefit
Inclusion criteria		relapse after treatment with SM1
Significant benefit Product A	Clinically relevant advantage based on **improved efficacy** **Qualitative**: SM1 (**add further line**) **Quantitative**: stronger effect in PFS with OS support SM2 (**direct** comparison) and SM3 (**indirect**)	

Hypothetical orphan at review - 2

Cancer B relapse	TKI X (2010) **parallel**	TKI Z SB required (2011)
Scientific evidence	**Placebo-controlled** (mPFS of placebo group: **12** mo) Primary EP: PFS **HR=0.5** OS not interpretable (cross-over) Subgroup with marker XY unresponsive	**Placebo-controlled** (mPFS of placebo group: **6** mo) Primary endpoint PFS **HR=0.3** OS numerical benefit; Benefit in subgroup with marker XY
Pretreatment history		… relapsed after treatment with **TKI X,** n had durable responses when treated with TKI B
Significant benefit TKI B	Clinically relevant advantage based on **improved efficacy** **Qualitative**: improved efficacy in subgroup (molecular marker + relapse after TKI X) **Quantitative**: stronger effect in PFS with OS support	

Hypothetical orphan at review - 3

Cancer B relapse	TKI X (2010) + 2 years	TKI Z SB required (2011).
Scientific evidence	**Placebo-controlled** (mPFS of placebo group: **10 mo** Primary EP: PFS **HR=0.7** OS not interpretable (cross-over) Subgr[illegible]arker XY unres[illegible]sive	**Uncontrolled or** (mPFS of placebo group: **12 mo** Primary endpoint PFS **HR=0.6** **OS not interpretable (cross-over)** **Safety profile different (how?)**
Pretreatment history		**Exclusion criterion:** **pre-treatment with TKI**

???

Lessons learned

- Protocol assistance highly recommended
- Demonstration of signficant benefit over „all authorised products“
    - Pre-treatment history
    - Identify subgroups unresponsive to authorised treatment
    - Carefully consider exclusion of certain prior/control treatments
- Claim of improved safety especially difficult
    - Not theoretical, should allow prospective patient selection
    - Frequency and relevance of AE important
- Totality of the data is assessed in context
    - Endpoints should reflect tangible benefit

Challenges

- Uncertainties with small numbers and typically single pivotal trials
- (Real!) parallel developments
- „Competitive areas“
    - Increasing requirements for the demonstration of SB
    - Best-in-class vs first-in-class
- Quantitative aspects of signficant benefit
    - Minimal effect size?
    - Time gained or Hazard Ratio?
    - Dependent on disease-related prognosis?
    - Further endpoints, esp. QoL?

Conclusions

- Heterogeneity of oncologic conditions and pharmacological treatment require case-by-case approach for maintenance of orphan designation
- More oncology OMPs require the demonstration of SB at the time of MA compared to orphans overall
- Most frequent ground for SB is a „clinically relevant advantage“ via „improved efficacy“
- Direct and indirect approaches
- Combination of categories for SB is possible and sometimes necessary
- Protocol assistance highly recommended

Thank you very much for your attention!

Thank the COMP and EMA orphan team and colleagues at BfArM for many fruitful discussions!

Questions?