Reimbursement Reality for Off-label use in Cancer Care – A systematic empirical investigation

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Introduction

Off-label drug use (OLU) is using drugs outside their approved indication and is common in oncology. Cancer drugs are expensive and their reimbursement is a challenge for health care systems, therefore OLU is partly regulated by reimbursement restrictions. In Switzerland, a reimbursement request needs to be issued before OLU treatment can be initiated. For evidence-based health care, OLU should be reimbursed in the case of sufficient evidence for a treatment benefit. However, little is known about factors that drive reimbursement decisions. We aim to investigate the relationship of the reimbursement decision with underlying evidence on treatment benefits.

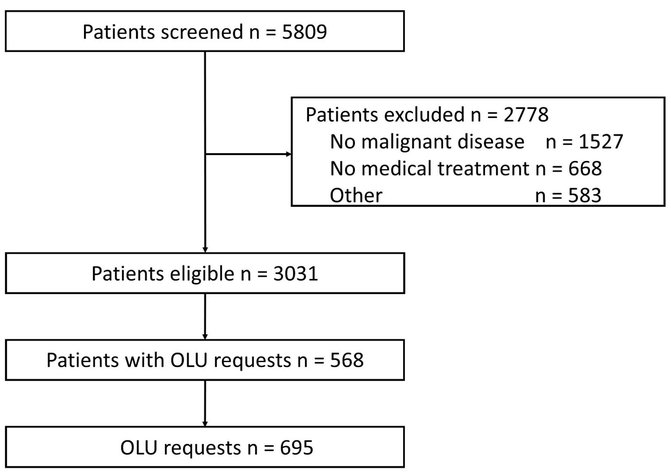

Figure 1: Flow Chart for Screening Process

Methods

- We used routinely collected health data (demographics, treatment & disease characteristics)
- For all reimbursement requests we extracted the correspondence with the health insurance and classified them request as on-label use or OLU
- OLU status was determined according to the Swissmedic label at the timepoint of the request
- Randomized trial evidence for treatment benefits at the timepoint of the request was determined using standard approaches for evidence synthesis

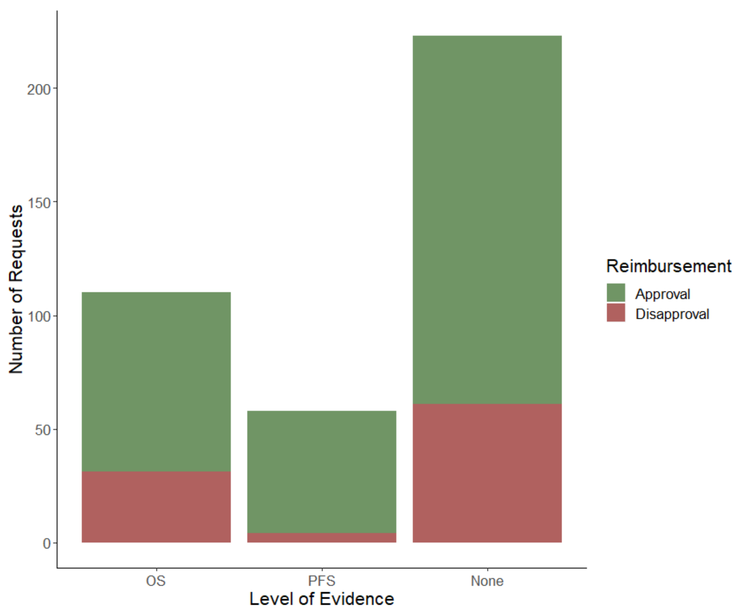

Figure 2: Number of requests according to the underlying evidence with the proportion of approval (green) and disapproval (red). Abbreviations: OS – Randomized trial evidence for overall survival, PFS – randomized trial evidence for progression-free survival; None – no randomized trial evidence for PFS or OS.

Results

Figure 1 - We screened records of 5809 patients. 568 (19%) of 3031 eligible patients had at least one reimbursement request for OLU.

Figure 2 - Randomized trial evidence indicates a survival benefit (OS) for 30% of intended OLU and better progression-free survival (PFS) for 15%. Requests were rejected in 30% of cases. We do not see an association between trial evidence for treatment benefits and reimbursement decisions.

Figure 3 and 4 - Reimbursement decisions by insurances are highly heterogeneous:
The odds of acceptance of reimbursement in the case of evidence for OS benefit varied substantially between different insurances. Reimbursement requests for indications with randomized evidence for OS benefit were partly rejected, while other indications with evidence only for PFS benefit were always accepted. Some indications are sometimes rejected or accepted within one insurance.

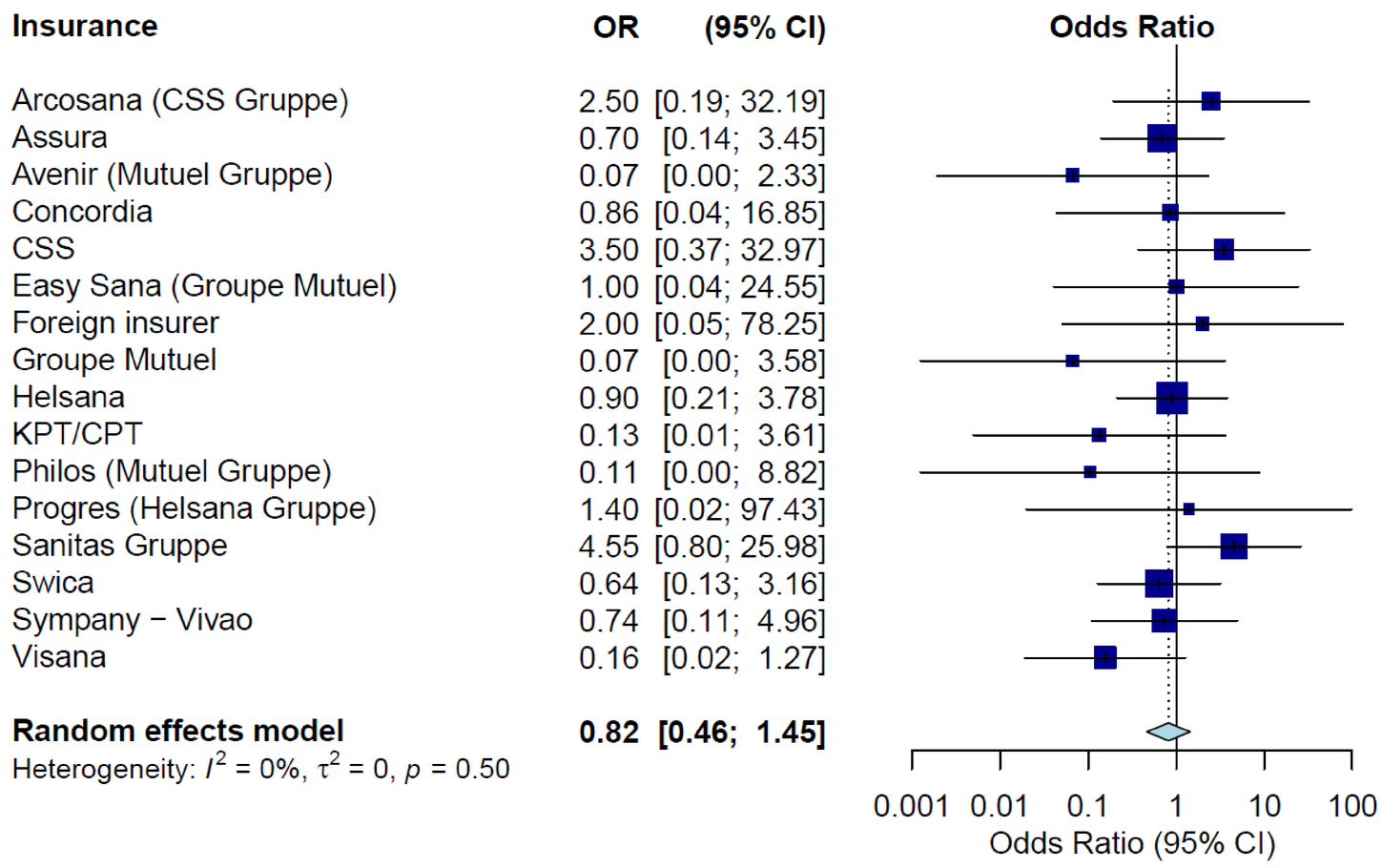

Figure 3: Forest plot of the OR for acceptance by single insurances. An OR >1 indicates a higher chance of acceptance for reimbursement requests in the case of trial evidence that indicates an OS benefit.

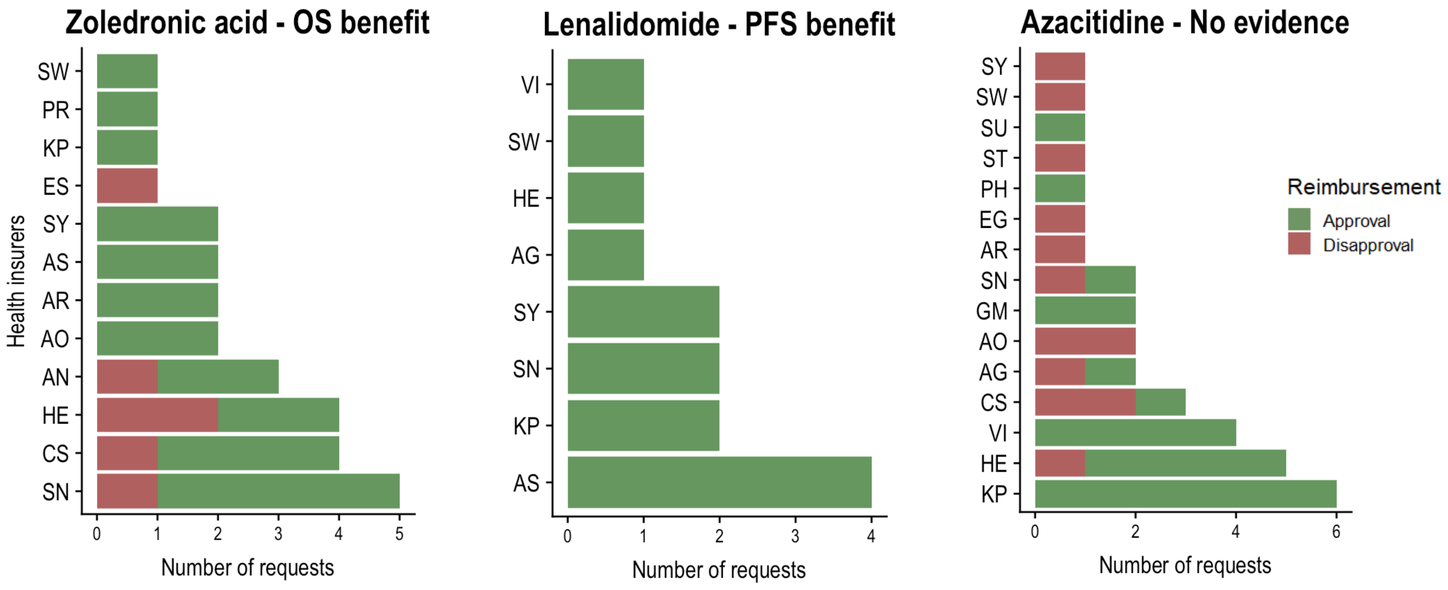

Figure 4: Proportion of approval (green) and disapproval (red) for three selected OLU indications: Zoledronic acid as adjuvant treatment for postmenopausal breast cancer; Lenalidomide as maintenance therapy in multiple myeloma and Azacitidine as maintenance after allogenic stem cell transplantation for acute myeloid leukaemia or myelodysplastic syndrome. The two letters stand for different health insurers.

Conclusions

- Our results indicate that randomized trial evidence for potential OS or PFS benefit does not drive reimbursement decision
- It remains unclear which factors drive reimbursement decision
- Uncertainty is increased by heterogeneity of reimbursement decisions between and within insurances

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