INTRODUCTION

We conducted a systematic literature review (SLR) with the aim of performing a network meta-analysis (NMA) to assess the safety of a new topical drug, tirbanibulin 1% ointment, compared with common treatments for actinic keratosis (AK) in Europe 1 (see Fig 1).

METHODS

In this poster we focus on the feasibility assessment (FA) that assessed the similarity of population, intervention, comparator, outcome and design among the eligible randomized controlled trials (RCTs). The outcomes of interest were related to the safety of tirbanibulin compared with other AK treatments.

RESULTS

• Of the 46 studies included in the SLR, six did not have sufficiently similar designs and populations or enough reported data to include in an NMA. Five studies assessed US rather than European posologies.

• Of the remaining 35 studies, only 22 studies reported data on discontinuations due to adverse events (AEs) or local skin reactions (LSRs).

• However, these 22 studies reported discontinuations across disparate populations, including intent-to-treat, per-protocol, safety, and completers.

• The 22 studies also defined disparate reasons for discontinuation, including any AE, local AEs, serious AEs, treatment-related AEs (TRAES), LSRs, serious TRAES, and local TEAES.

• Direct comparison of discontinuations between studies was therefore difficult; to resolve this, the network was limited to the comparable sub-set deemed most clinically relevant (discontinuations due to TEAES, TRAES, local AEs or LSRs) – see Fig 2.

• However, in this network data were extremely sparse (most arms had low discontinuations or even no discontinuations, i.e., were uninformative for a Bayesian NMA).

• Both tirbanibulin trials had zero discontinuations in both placebo/vehicle and treatment arms, i.e., were uninformative. It was therefore impossible to estimate relative treatment effects between tirbanibulin and other treatments under a binomial model, so NMA was not the best method to compare tirbanibulin with other treatments.

• Instead, data on discontinuations were compared qualitatively. Eligible interventions generally reported low rates of 2% or below, including tirbanibulin with 0%, and placebo/vehicle with rates between 0 and 0.6%. Two of the interventions (fluorouracil 0.5% + salicylic acid and diclofenac sodium 3%) reported rates between 6 and 9%.

• Data on the incidence of at least one severe LSR following treatment were insufficient to create a network. Tirbanibulin, fluorouracil 0.5% + salicylic acid and diclofenac sodium 3% showed low severe LSR rates (≤11%), whilst imiquimod showed higher rates (severe redness 31%, severe erythema 25%).

CONCLUSIONS

• Although AEs and LSRs and resulting discontinuations were a key outcome of interest, a lack of reporting, lack of homogeneity in reporting, and methodological challenges hindered any in-depth comparison of these safety data.

• FA is a useful tool to identify issues with data reporting and quality, and to determine whether to compare data quantitatively or summarize qualitatively.

• Qualitative comparisons in the absence of direct evidence should be interpreted with caution – they are unable to account for heterogeneity between studies, and ignore any potential effect modifiers.

REFERENCES
