Efficacy of targeted drugs for the treatment of adults with moderate-to-severe plaque psoriasis in the Russian Federation: a systematic literature review update

Tolkacheva D.G., Sokolova V.D., Sableva N.A., Mladov V.V.

BACKGROUND

According to clinical guidelines, there is a number of targeted drugs for the treatment of adult patients with plaque psoriasis. Numerous placebo-controlled randomized clinical trials (RCTs) have been conducted in order to evaluate their efficacy in adult suffering from moderate-to-severe plaque psoriasis. Although direct comparisons between drugs are not common. The first systematic review and network meta-analysis assessing efficacy and safety of targeted drugs for adult patients with moderate-to-severe plaque psoriasis in the Russian Federation was published in 2019.

OBJECTIVES

To update the existing systematic review and network meta-analysis comparing the efficacy of targeted drugs in adults with moderate-to-severe plaque psoriasis by adding randomized clinical trials (RCTs) on a new interleukin (IL) 23 inhibitor registered in the Russian Federation – risankizumab, and other RCTs published after 2019.

METHODS

We updated our systematic literature search in PubMed/MEDLINE and Embase databases. Evidence synthesis included RCTs evaluating the efficacy of adalimumab (ADA), infliximab (INF), etanercept (ETN), certolizumab pegol (CZP), ixekizumab (IXE), netakimab (NTK), secukinumab (SEC), risankizumab (RIS), guselkumab (GUS), ustekinumab (UST), tofacitinib (TOFA), and apremilast (APR) after 12 weeks of therapy. The Bayesian meta-analyses with meta-regression accounted for high heterogeneity in patient characteristics and significant differences in placebo response rates. The considered drugs were ranked based on values of surface under the cumulative ranking curve (SUCRA). Additionally, drug class analyses were carried out.

RESULTS

Twenty-three new RCTs were added to the network. For all efficacy outcomes, we interpreted the results of random effects models adjusted to response in the placebo group taking into account the identified heterogeneity between RCTs.
IL-23 inhibitor RIS, recently approved in Russia, has joined the group of the most efficacious drugs, such as IL-17 inhibitors NTK and IXE, as well as IL-23 inhibitor GUS. In terms of PASI 75, RIS and IXE showed superiority compared to tumor necrosis factor-alpha (TNFα) inhibitors (INF, ADA, ETN), small molecules (TOFA and APR), and IL-12/23 inhibitor UST, while NTK and GUS were characterized by comparable efficacy with INF and outperformed the remaining drugs. Adding new SEC studies increased the power of analysis and allowed this drug to demonstrate comparable efficacy with NTK, RIS, IXE and GUS as well as superiority over all IFNα, except for IFN and iIL-12/23 UST. There were no statistically significant differences between all the TNFα inhibitors.
Drug class analyses revealed that IL-23 inhibitors and IL-17 inhibitors occupied the highest ranks for all efficacy outcomes and demonstrated superiority in efficacy over IL-12/23 inhibitors, TNFα inhibitors and small molecules. At the same time, IL-12/23 and TNFα inhibitors were characterized by comparable efficacy.

CONCLUSION

The addition of head-to-head trials and increased statistical power of the network revealed previously unidentified significant differences between treatment options for moderate-to-severe plaque psoriasis.
Research results may be useful for healthcare professionals' decision-making process about the optimal therapy for adult patients with moderate-to-severe plaque psoriasis. Presented data can become the basis of pharmacoeconomic studies for drug reimbursement or for decision-making process about drug procurement them at regional or hospital level. The results may lead to an increase in prescription of
IL-17 and IL-23 inhibitors as the most efficacious treatment options for moderate-to-severe plaque psoriasis.

DISCUSSION

Analysis by classes demonstrated strong correlation with RWE practice, IL inhibitors showed higher efficacy compared to TNF inhibitors, who demonstrated a decrease in therapeutic response in the long-term. In majority of RCTs estimation of the time till response varies from 10 to 16 weeks or even after 16 weeks, which may be associated with the reduction in drug regimen.

The choice of first-line therapy and the place of biologics in the treatment of moderate-to-severe plaque psoriasis in the Russian Federation remain debatable. Biologics are used as a third-line therapy, reimbursement program suffers from the lack of transparency and budget limitations.

General network diagram
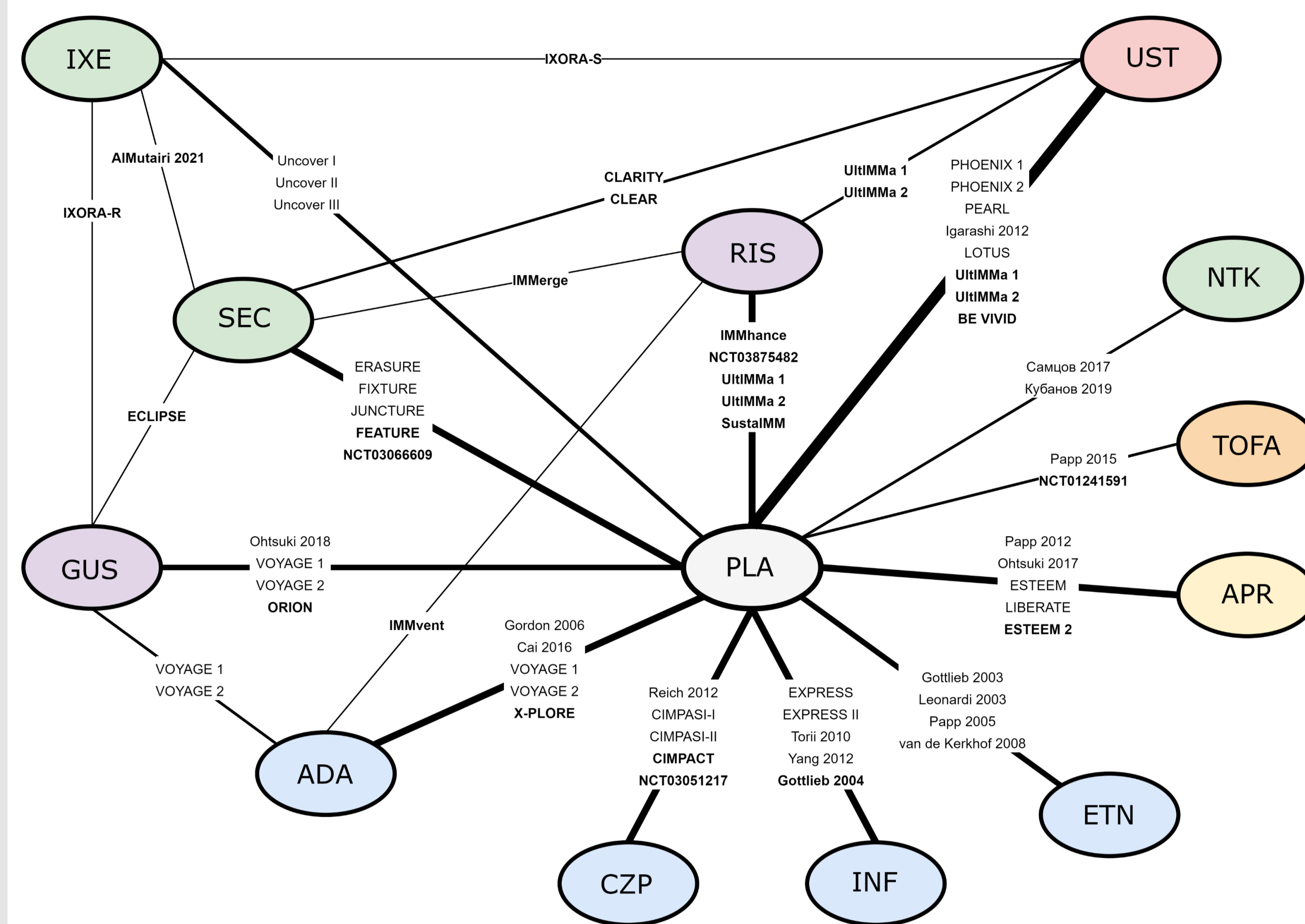
SUCRA

	PASI 75	PASI 90	PASI 100	PGA/IGA 0/1	DLQI
IXE	90,9	97,6	97,3	90,2	80,1
RIS	92,5	86,8	79,9	86,5	79,7
GUS	75,4	80,9	60,4	76,8	68,7
SEC	77,7	80,5	67,0	69,1	38,9
NTK	83,7	75,2	67,7	62,7	НД
INF	63,4	62,7	14,5	96,2	12,7
RIS	32,9	36,8	НД	36,2	97,4
ADA	42,6	47,6	27,9	45,6	36,8
UST	44,9	47,4	34,0	48,4	23,1
CZP 200	48,5	39,1	НД	39,9	54,8
ETN 50	20,5	16,4	НД	20,6	49,9
APR	10,1	15,3	НД	9,2	66,0
ETN 25	17,1	14,9	НД	17,5	41,9
PLA	0,0	0,0	0,0	0,0	0,0

SUCRA
0   25   50   75   100

Table of pooled values of risk ratio (RR) and credible interval of efficacy based on PASI 75 and PASI 90 for 12 weeks