ABSTRACT NUMBER: 1745

Use of Statins and Its Association with Major Adverse Cardiovascular Outcomes with Tofacitinib versus TNF Inhibitors in a Risk-Enriched Population of Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Date: Sunday, November 17, 2024

Session Type: Abstract Session

Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes III: Best Day (RA Subpopulations)

Session Time: 3:00PM-4:30PM

Background/Purpose: ORAL Surveillance (NCT02092467; a post-authorization safety study of tofacitinib 5 and 10 mg twice daily [BID] vs TNF inhibitors [TNFi]) found higher incidence of major adverse cardiovascular (CV) events (MACE) with tofacitinib vs TNFi. A previous analysis of the study indicated that the risk difference was primarily found in patients (pts) with history of atherosclerotic CV disease (ASCVD) and also observed low frequency of baseline statin use. Current management guidelines recommend a high-intensity statin for pts with history of ASCVD or a high 10-year predicted risk of MACE (CV risk), and a moderate-intensity statin for pts with intermediate CV risk.

In this post hoc analysis, we aimed to clarify (1) statin usage by baseline CV risk profile, (2) the impact of statins on lipid levels, and (3) the association between statin use and incident MACE with tofacitinib vs TNFi in ORAL Surveillance.

Methods: Pts with RA aged ≥50 years and ≥1 additional CV risk factor received tofacitinib 5 mg (N=1455) or 10 mg (N=1456) BID, or TNFi (N=1451). Use of statins was assessed at baseline and during the study and classified as high-, moderate-, or low-intensity statin treatment. Low- and high-density lipoproteins (LDL and HDL) were determined in fasting serum. Hazard ratios (HRs; time to first event analysis) and 95% confidence intervals (CI) were evaluated based on simple Cox proportional hazard models.

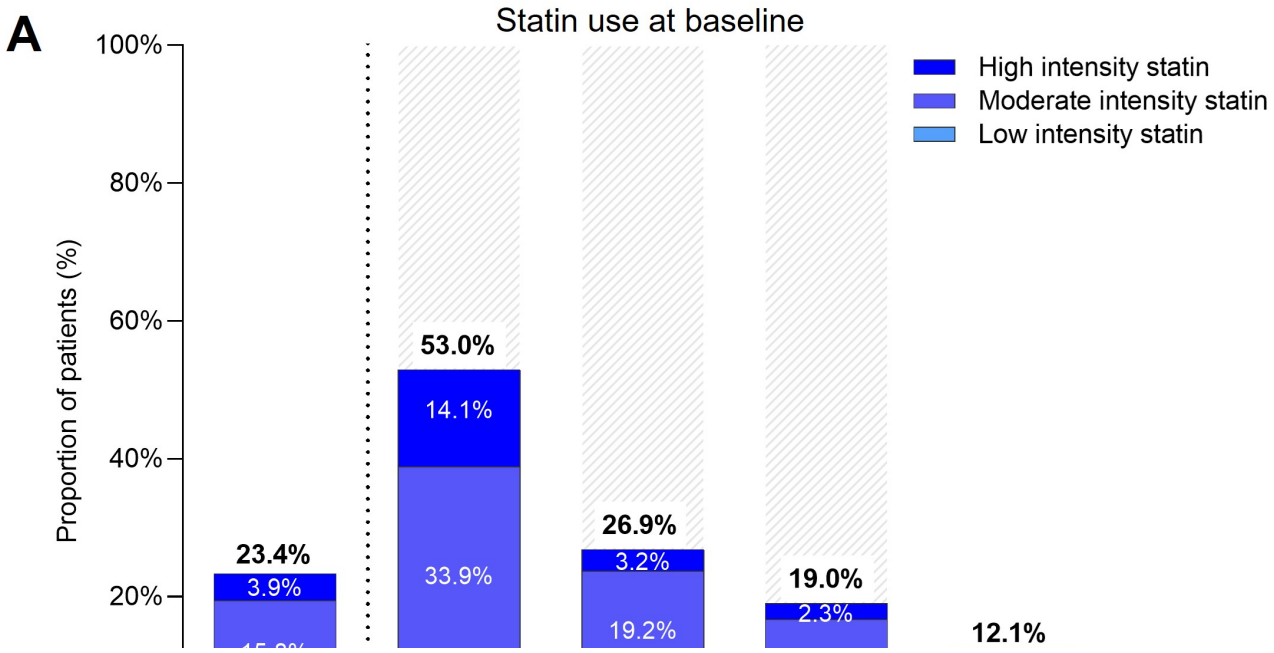
Results: Among pts with history of ASCVD or high CV risk, 53.0% and 26.9%, respectively, used a statin at baseline (Figure 1A). Few of these used a high intensity statin. 19.0% of pts with intermediate CV risk received a statin at baseline, predominantly a moderate-intensity statin (Figure 1A). Baseline statin use was similar in tofacitinib and TNFi treated pts. Initiation of a statin during the study was observed in relatively few pts and more frequently with tofacitinib (11.8% [5 mg BID] and 12.2% [10 mg BID]) than with TNFi (6.7%) (Figure 1B).

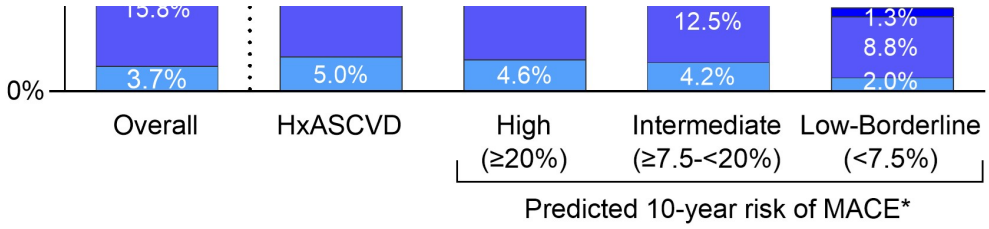
Baseline LDL and the LDL:HDL ratio were lower in pts using a statin (Figure 2). In pts with or without statins, LDL and HDL increased from baseline and to a larger extent with tofacitinib than with TNFi (Figure 2).

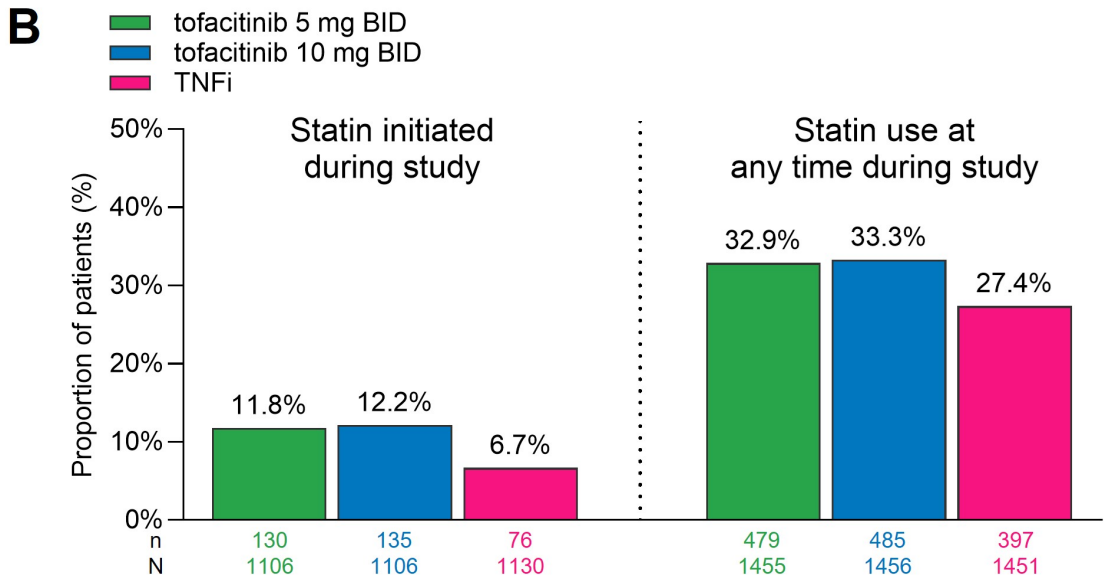
In the overall study population and across treatments, MACE rates were similar in pts with or without baseline statin use (data not shown). Among tofacitinib-treated pts with history of ASCVD, occurrence of MACE over follow-up was lower in pts using statins at any time vs those without statin use (HR 0.49 [95% CI 0.25, 0.95]) (Figure 3). This pattern was not observed in TNFi-treated pts with history of ASCVD. Among pts with ASCVD history and no use of statins at any time, occurrence of MACE was higher with tofacitinib vs TNFi (HR 4.07 [95% CI 1.20, 13.82]). In pts with ASCVD history and use of statins at baseline or at any time there did not appear to be a difference in incident MACE with tofacitinib vs TNFi (HR 1.17 [95% CI 0.48, 3.00]) (Figure 3).

Conclusion: This post hoc analysis of ORAL Surveillance emphasizes that there is a gap in the CV preventive care of pts with RA, as evident from inadequate use of statins. Among pts with history of ASCVD, use of statins appears to be critical in mitigating the previously reported MACE risk observed to accompany tofacitinib use vs TNFi.

Figure 1. Use of statins during ORAL Surveillance.

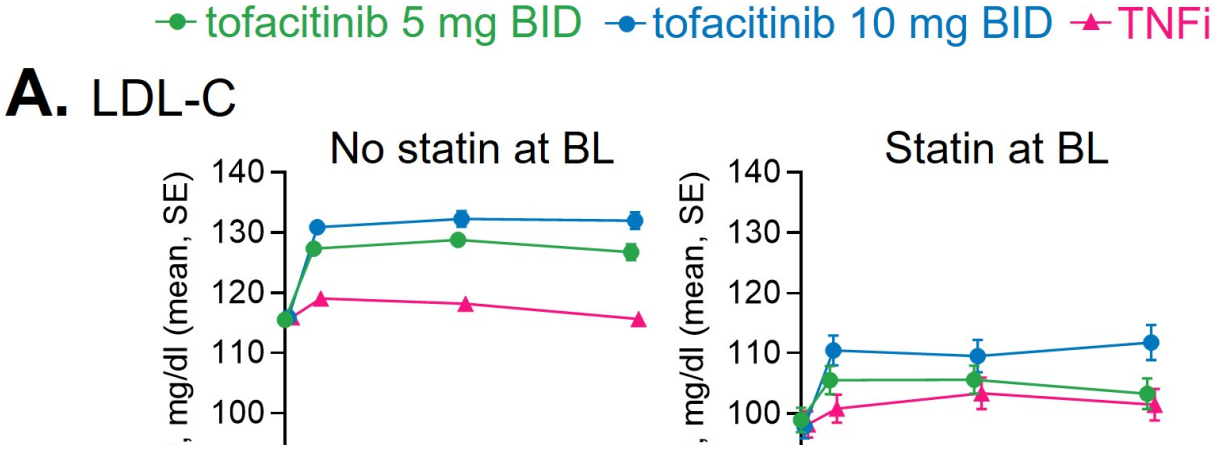


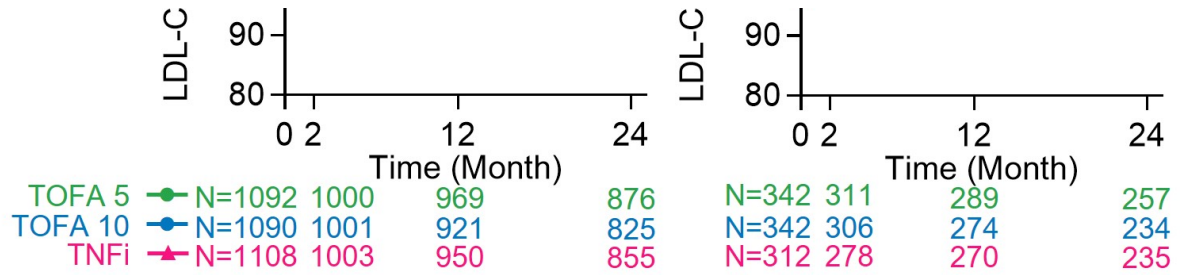


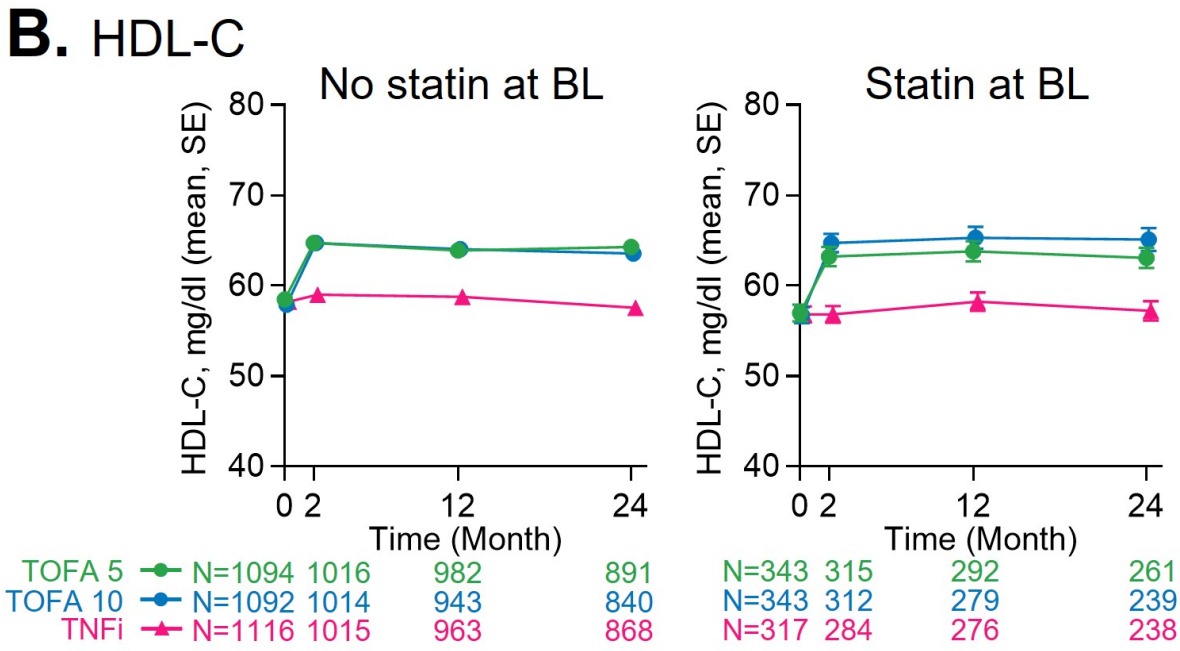


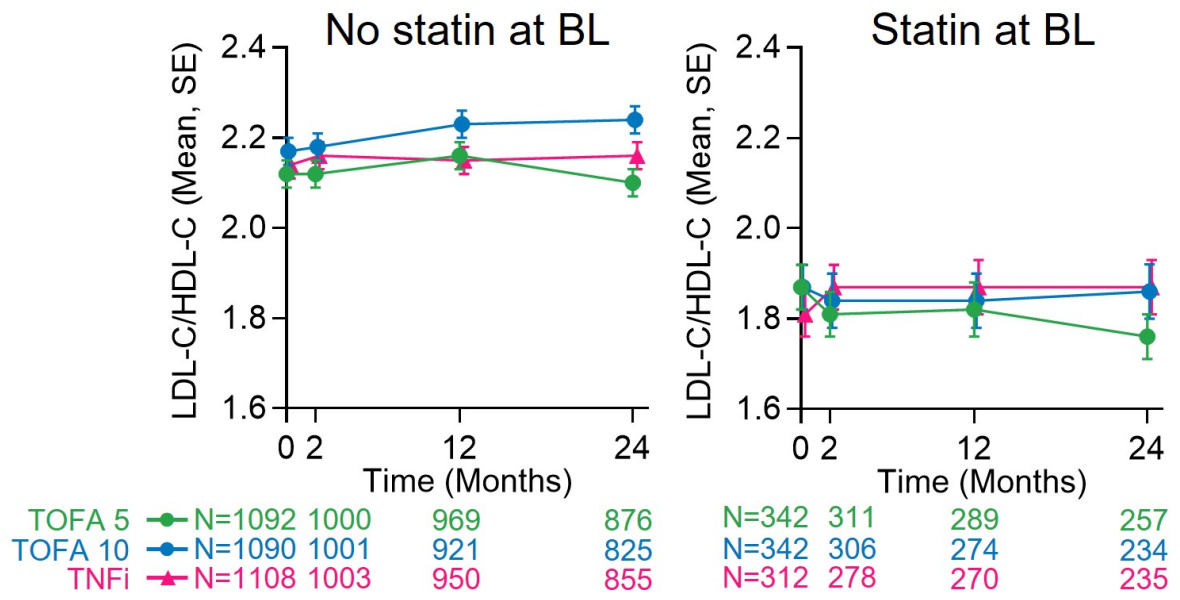
Statin use at baseline in the overall study population (A) was based on day 1 of treatment with tofacitinib or TNFi and was categorized by intensity based on type of statin and daily dose. Shaded area of bar graphs indicates target use of statin by CV risk category (given no contraindication) by 2018 AHA/ACC blood cholesterol management guideline (Grundy et al., J Am Coll Cardiol 2019; 73:e285-e350). *In patients with no history of ASCVD, 10-year risk of MACE was calculated with the ASCVD-PCE calculator, and a 1.5 multiplier was applied for RA, as recommended by EULAR. Statin initiated during study (B) reflects use of statin in patients with no reported statin on day 1 of study. Statin use at any time excluded usage that was <30 days and usage that was initiated within 90 days of MACE event for subjects with any MACE event.
BID, twice daily; BL, baseline; HxASCVD, history of atherosclerotic cardiovascular disease; MACE, major adverse cardiovascular events; n, number of patients with events; N, number of evaluable patients; TNFi, tumor necrosis factor inhibitor.

Figure 2. Impact of tofacitinib vs TNFi on levels of LDL-C and HDL-C and LDL-C/HDL-C ratio in patients without and with statin treatment at baseline.



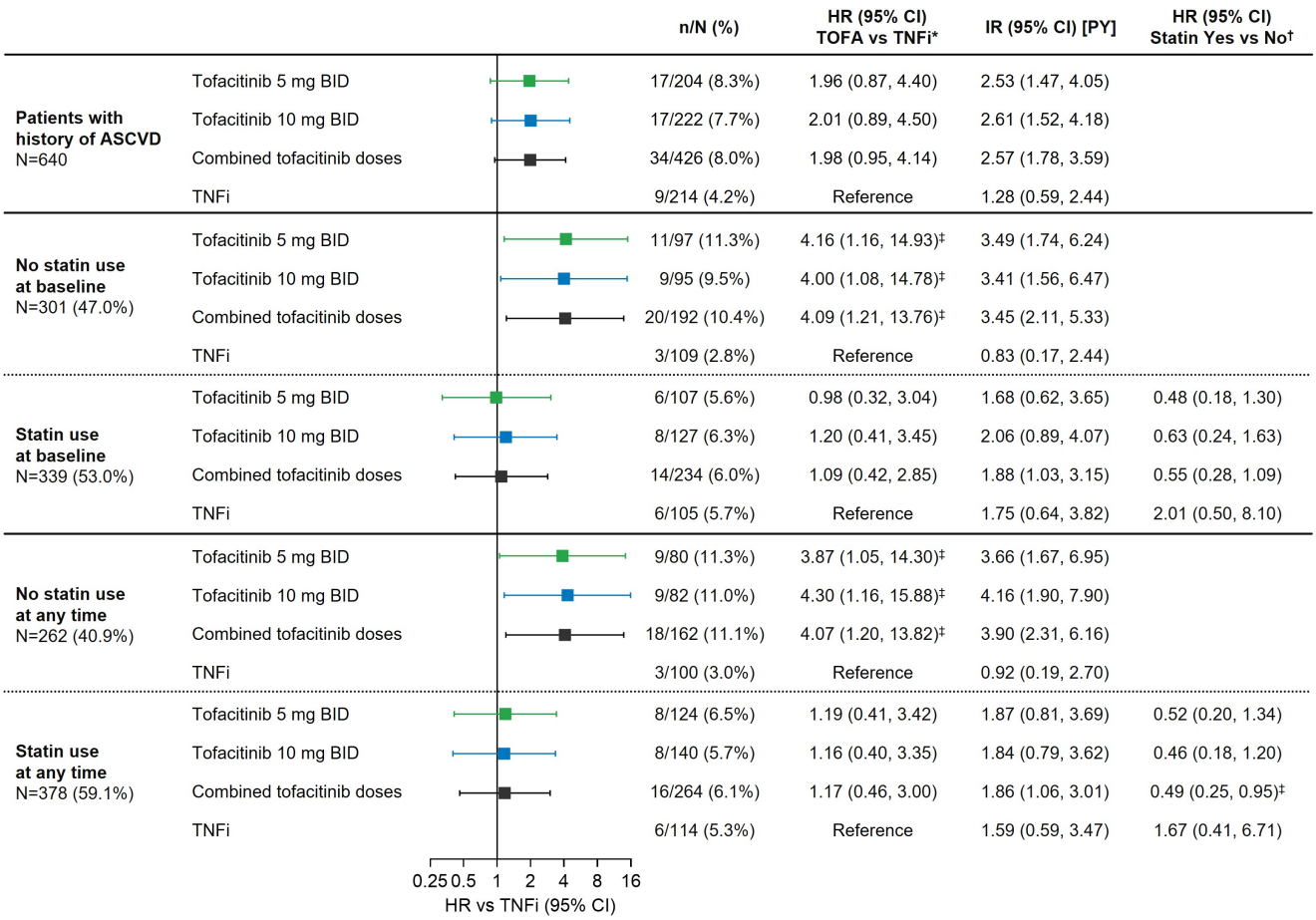






Serum lipids were determined in fasting blood samples. Statin use at baseline was based on day 1 of treatment with tofacitinib or TNFi. BL, baseline; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; SE, standard error; TOFA 5, tofacitinib 5 mg BID; TOFA 10, tofacitinib 10 mg BID; TNFi, tumor necrosis factor inhibitor.

Figure 3. Occurrence of MACE with tofacitinib vs TNFi in patients with history of ASCVD by use of statin.



Statin use at baseline was based on day 1 of treatment with tofacitinib or TNFi. Statin use at any time excluded usage that was <30 days and usage that was initiated within 90 days of MACE event for subjects with any MACE event. HRs are shown on a logarithmic scale. IRs express number of patients with first events per 100 PY.
*HR vs TNFi (95% CI) is based on two simple Cox proportional hazard models (one for comparing combined tofacitinib doses vs TNFi, and the other for comparing tofacitinib 5 and 10 mg BID vs TNFi), with treatment as the only covariate. †HR (95% CI) of statin Yes vs No is based on a Cox model with use of statins as only covariate performed within each treatment group. ‡HR 95% CI excludes 1.
ASCVD, atherosclerotic cardiovascular disease; BID, twice daily; CI, confidence interval; HR, hazard ratio; IR, incidence rate; MACE, major adverse cardiovascular events; n, number of patients with events; N, number of evaluable patients; PY, patient-years; TOFA, tofacitinib; TNFi, tumor necrosis factor inhibitor.

Disclosures: J. Giles: AbbVie, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2; **c. Charles-Schoeman**: AbbVie/ Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2; **M. Buch**: AbbVie, 2, 6, Arxx Therapeutics, 2, Boehringer Ingelheim, 6, CESAS Medical, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, Medistream, 6, Pfizer, 2, 6; **M. Dougados**: AbbVie/Abbott, 1, 5, Eli Lilly, 1, 5, Gilead, 1, 5, Janssen, 1, 5, Merck/MSD, 1, 5, Novartis, 1, 5, Pfizer, 1, 5, UCB, 1, 5; **Z. Szekanecz**: AbbVie/Abbott, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 1, 2, 6, Gedeon Richter, 1, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi, 2, 6; **T. Mikuls**: Elsevier, 9, Horizon Therapeutics, 2, 5, Pfizer, 2, Sanofi, 2, UCB Pharma, 2, Wolters Kluwer Health (UpToDate), 9; **S. Ytterberg**: Corbus Pharmaceuticals, 2, Kezar Life Sciences, 2, Pfizer, 1, 2; **G. Koch**: AbbVie/Abbott, 5, Acadia Pharmaceuticals, 5, Aerovant Therapeutics, 5, Amgen, 5, AstraZeneca, 5, Bayer, 5, Cytokinetics, 5, Galderma Research Development, 5, Gilead, 5, GlaxoSmithKline, 5, HUYA Bioscience International, 5, Intracellular Therapies, 5, Johnson & Johnson, 5, Momentum, 5, Otsuka, 5, Pfizer, 1, 5, Regeneron Pharmaceuticals, 5, Scholar Rock, 5, Summit

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