**Appendix Table D42. Randomized controlled clinical trials that examined efficacy of beta-blockers for migraine prevention in adults**

| **Reference**  **Aim** | **Total Sample [Number Analyzed] % Females in Sample** | **Definition of Migraine** | **Duration of Migraine** | **Presence of Aura** | **Migraine Frequency at Baseline/Month** | **Age of Subjects (Mean or Median)** |
| --- | --- | --- | --- | --- | --- | --- |
| Ekbom, 197288 To investigate the effect of beta-receptor blocking agents on migraine by using a new compound, LB-46 (d,1-4-indol) | 30 [26] 86.7 | Ad Hoc Committee, 1962 | Not reported | Since 4 had classic migraine it was assumed that these patients had migraine with aura | 4 | Mean 33.7 years |
| Sjaastad, 197289 To test the efficacy of Visken (LB-46) in migraine prophylaxis with a double-blind technique | 28 [24] 85.7 | Ad Hoc Committee on classification of headache (1962) | Not reported | Since 14 patients had classical migraine it was assumed that they had migraine with aura | 2 | Mean 35.8 years |
| Ekbom, 197590 Not reported | 33 [28] 81.8 | Ad Hoc Committee on classification of headache and World Federation of Neurology’s Research Group on Migraine and Headache | Not reported | Since 6 patients had classic migraine it was assumed that these patients had migraine with aura | 3 | Mean 41.3 years |
| Nanda, 197891 Not reported | 43 [33] 74.4 | Migraine with the following characteristics: 1) Onset of first attack before age 25 years; 2) No evidence of a progressive neurological deficit over three years; 3) Hemicrania in association with any two of the following: a) family history, b) nausea and vomiting, and c) psychic, visual, or sensory prodroma | Not reported | Not reported | 4.8 | Not reported |
| Briggs, 197992 To assess the value of timolol in migraine prophylaxis and to elucidate further the reason for the varied response to different beta-blockers. | 14 [Variable] 71.4 | Ad Hoc Committee on classification of headache | Not reported | Since 2 patients had classical it was assumed that these patients had migraine with aura | 2 | Not reported |
| Ryan, 198293  Ryan, 198394  To determine the relative efficacy and safety of nadolol in reducing the frequency and/or the severity of migraine attacks as compared to placebo | 80 [80] 77.5 | Not reported | Not reported | Not reported | 3 | Not reported |
| Forssman, 198295  Forssman, 198396 To confirm the use of atenolol in migraine prophylaxis in a double-blind cross-over study with placebo | 24 [20] 80.0 | Ad Hoc Committee on classification of headache | Not reported | Since the definition of migraine was according to the Ad Hoc Committee classification it was assumed that none of the patients had aura | Not reported | Mean 40 years |
| Andersson, 198397 To evaluate whether metoprolol decreases 1) the frequency, 2) the severity of the migraine attacks, 3) days with migraine, 4) consumption of acute migraine medication, compared with placebo in patients with classical and non-classical migraine | 71 [65] 84.5 | Vahlquist’s criteria and World Federation of Neurology Research Group on Migraine and Headache | 18.4 years | Not reported | 4.8 | Mean 39.7 years |
| Stellar, 198479 To compare timolol with placebo | 107 [94] 72.0 | Ad Hoc Committee on Classification of Headache. | Not reported | Since 5 patients had classic migraine it was assumed that they had migraine with aura. | 3 | Mean 43 years |
| Freitag, 198498 To evaluate the efficacy of nadolol in reducing the frequency and severity of migraine headaches | 32 [32] 81.3 | Ad Hoc Committee on classification of headache | Not reported | Not reported | Not reported | Mean 36.3 years |
| Johannsson, 198799 To investigate the prophylactic anti-migraine effect of atenolol, a cardiovascular, water-soluble beta-antagonist | 72 [63] 69.8 | Ad Hoc Committee on classification of headache | 26 years | Since the definition of migraine was according to the Ad Hoc Committee classification it was assumed that none of the patients had aura | 2 | Mean 43 years |
| Kangasneimi, 1987100 To compare metoprolol with placebo in patients with frequent classic migraine attacks | 77 [74] 79.7 | NIH Ad Hoc Committee | 17.2 years | Since all had classic migraine it was assumed all had migraine with aura | 4.3 | Mean 37.5 years |
| van de Ven, 1997101 To assess the efficacy of bisoprolol in migraine prophylaxis | 226 [Not reported] 82.0 | Not reported | Age at onset (years): 20.3 | 23% of patients had migraine with aura and 77% migraine without aura | 5.5 | Mean 38.7 years |
| Siniatchkin, 2007102 To investigate the influence of a controlled-release (CR) form of metoprolol on the amplitude and habituation of the early and late control negative variation (CNV) components using a double-blind, placebo-controlled, parallel-group design with systematic multiple CNV recordings during the treatment phase in order to provide more complete analysis of the treatment process. | 20 [20] 85.0 | International Headache Society criteria | 22.3 years | One of the inclusion criteria was patients having migraine without aura | 4.6 | Mean 37 years |