

Additional file 3: Detailed adverse event outcomes in each trial

| Study # condition duration | Patients and methods | Dosing regimen, numbers of patients | Withdrawals | | | Adverse Events | | | | | | | |
|----------------------------------|--|---|--|---|--|---|--|---|--|---|--|---|--|
| | | | All causes | Lack of Efficacy | Adverse event | General | GI-related | GI tolerability | Cardiorenal-related | Laboratory Tests | Treatment- related | | |
| Osteoarthritis | | | | | | | | | | | | | |
| C-002 OA 12 weeks | OA Hip/Knee (ACR), requiring NSAID, and with stable controlled hypertension and Type 2 diabetes FCC 1-3 Washout 7-10 days Double dummy method Assessed at baseline, 6, 12 weeks QS 5/5; VS 16/16 | Cele 1x200mg/day (n=136) Role 1x25mg/day (n=132) Naprox 2x500mg/day (n=128) | Cele 30/136 Role 37/132 Naprox 32/128 | Cele 3/136 Role 1/132 Naprox 3/128 | Cele 6/136 Role 13/132 Naprox 10/128 | Any AE: Cele 72/136 Role 71/132 Naprox 73/128 GI-related: Cele 1/136 Role 1/132 Naprox 4/128 Serious: Cele 4/136 Role 5/132 (1 MI, 1 aggravated hypertension) Naprox 3/128 Serious UGI: None | Dyspepsia: Cele 1/136 Role 1/132 Naprox 1/128 Abdom Pain: Cele 5/136 Role 5/132 Naprox 7/128 Nausea: Cele 4/136 Role 7/132 Naprox 8/128 Diarrhoea: Cele 6/136 Role 10/132 Naprox 4/128 Vomiting: Cele 1/136 Role 2/132 Naprox 1/128 | Duodenal Ulcer: Cele 1/136 Role 0/132 Naprox 0/128 Gastric erosion: Cele 5/136 Role 11/132 Naprox 9/128 | Mod/severe abdom pain, nausea, dyspepsia: Cele 5/136 Role 10/132 Naprox 4/128 Elevated systolic BP: Cele 10/132 Role 3/132 Naprox 2/128 Facial oedema: Cele 1/136 Role 0/132 Naprox 0/128 Ankle oedema: Cele 1/136 Role 0/132 Hypertension: Cele 1/136 Role 0/132 Aggravated hypertension: Cele 0/136 Role 3/132 Naprox 3/128 MI: Cele 0/132 Role 1/132 Naprox 0/128 | From treatment emergent AEs Oedema: Cele 1/136 Role 3/132 Naprox 2/128 Facial oedema: Cele 1/136 Role 0/132 Naprox 0/128 Ankle oedema: Cele 1/136 Role 0/132 Hypertension: Cele 1/136 Role 0/132 Aggravated hypertension: Cele 0/136 Role 3/132 Naprox 3/128 MI: Cele 0/132 Role 1/132 Naprox 0/128 | Non-significant decreases in Hb in each group | All AEs: Cele 5/136 Role 13/132 Nap 13/128 Serious: Cele 0/136 Role 2/132 Naprox 0/128 | |
| C-003 OA 6 weeks | OA knee (ACR) with flare, requiring daily NSAID/analgesic FCC 1-3 Washout 2 days Double dummy method Assessed at baseline, 3, 6 weeks QS 5/5; VS 16/16 | Cele 1x200mg/day (n=189) Role 1x25mg/day (n=190) Naprox 2x500mg/day (n=96) | Cele 31/189 Role 29/190 Plac 34/98 | Cele 10/189 Role 10/190 Plac 21/96 | Cele 11/189 Role 10/190 Plac 5/96 | Any AE: Cele 82/189 Role 80/190 Plac 29/92 GI-related: Cele 5/189 Role 3/190 Plac 1/96 Serious: Cele 3/189 Role 1/190 Plac 3/96 Serious UGI: Cele 0/189 Role 0/190 Plac 1/96 (GIH) | Dyspepsia: Cele 11/189 Role 10/190 Plac 30/96 Abdom Pain: Cele 5/189 Role 2/190 Plac 2/96 Nausea: Cele 1/189 Role 3/190 Plac 1/96 Diarrhoea: Cele 8/189 Role 5/190 Plac 1/96 Vomiting: Cele 1/189 Role 0/190 Plac 0/96 | GI Haemorrhage: Cele 0/189 Role 0/190 Plac 1/96 No ulcers or erosions | Mod/severe abdom pain, nausea, dyspepsia: Cele 6/189 Role 7/190 Plac 2/96 | Peripheral oedema: Cele 5/189 Role 8/190 Plac 2/96 Generalised oedema: Cele 1/189 Role 3/190 Plac 0/96 Hypertension: Cele 1/189 Role 6/190 Plac 0/96 Aggravated hypertension: Cele 1/189 Role 0/190 Plac 1/96 | Trial did not report any cases of heart failure | No patient withdrew due to clinically relevant laboratory values | All AEs: Cele 17/189 Role 15/190 Plac 4/96 Serious: Cele 1/189 Role 0/190 Plac 0/96 |
| C-010 OA 6 weeks | Symptomatic OA hip/knee, K-L 2-4, requiring NSAID/analgesic Initial pain intensity 40-90 on 100mm VAS Washout 3 days or 5 x half-life No investigational medication >30 days Doble dummy method Assessed at baseline, 6 weeks QS 5/5; VS 16/16 | Cele 1x200mg/day (n=181) Para 4x1000mg/day (n=171) VAS Plac (n=172) 1st treatment period analysed | Cele 42/181 Para 42/171 Plac 50/172 | [consent withdrawn] Cele 14/181 Para 17/171 Plac 24/172 | Any AE: Cele 11/181 Para 15/171 Plac 12/172 GI-related: Cele 5/181 Para 6/171 Plac 2/172 Serious: Cele 0/181 Para 2/171 Plac 3/172 Serious UGI: Cele 0/181 Para 0/171 Plac 1/172 | Any AE: Cele 74/181 Para 75/171 Plac 17/172 GI-related: Cele 3/181 Para 5/171 Plac 4/172 Diarrhoea: Cele 6/181 Para 14/171 Plac 4/172 Abdom Pain: Cele 1/181 Para 4/171 Plac 3/172 Vomiting: Cele 1/181 Para 4/171 Plac 4/172 | Mod/severe abdom pain, nausea, dyspepsia: Cele 6/181 Para 7/171 Plac 2/172 | Periph Oedema: Cele 1/181 Para 0/172 Plac 0/172 Aggravated hypertension: Cele 0/181 Para 1/171 Plac 0/172 | Cardiac failure: Trial did not report any cases | Group mean data given Hct values unchanged in period 1. Very small changes in mean hb values with no sig difference between groups | All AEs: Cele 24/181 Para 22/171 Plac 13/172 No serious AEs were related to the study medication | | |
| C-013 OA 2 weeks | OA (ACR) with flare FCC 1-3 Assessment at baseline, 1, 2 weeks Washout 2-14 days Double dummy method Assessed at baseline, 6 weeks QS 5/5; VS 16/16 | Cele [1] 2x40mg/day (n=73) Cele [2] 2x100mg/day (n=75) Cele [3] 2x200mg/day (n=73) Plac (n=70) | Cele [1] 9/73 Cele [2] 9/75 Cele [3] 6/73 Plac 15/70 | Cele [1] 6/73 Cele [2] 1/75 Cele [3] 3/73 Plac 10/70 | Cele [1] 0/73 Cele [2] 5/75 Cele [3] 3/73 Plac 2/70 GI-related: Cele [1] 0/73 Cele [2] 1/75 Cele [3] 0/73 Plac 1/70 Serious: Cele [1] 0/73 Cele [2] 1/75 Cele [3] 1/75 Plac 0/70 Serious UGI: None reported Serious CV: Cele [1] 0/73 Cele [2] 0/75 Cele [3] 1/73 Plac 0/70 No vomiting reported | Any: Cele [1] 30/73 Cele [2] 35/75 Cele [3] 36/73 Cele [3] 30/70 GI-related: Cele [1] 0/73 Cele [1] 10/73 Cele [2] 15/75 Cele [3] 14/73 Plac 10/70 Nausea: Cele [1] 2/73 Cele [2] 3/75 Cele [3] 3/73 Plac 7/70 Abdom pain: Cele [1] 2/73 Cele [2] 2/75 Cele [3] 4/73 Plac 10/70 Nausea: Cele [1] 3/73 Cele [2] 5/75 Cele [3] 2/73 Plac 0/70 Diarrhoea: Cele [1] 5/73 Cele [2] 3/75 Cele [3] 6/73 Plac 2/70 No vomiting reported | Mod/severe abdom pain, nausea, dyspepsia: Cele [1] 7/73 Cele [2] 3/75 Cele [3] 5/73 Plac 5/70 | Peripheral oedema: Cele [1] 1/73 Cele [2] 1/75 Cele [3] 0/73 Plac 0/70 No report of hypertension, MI or CHF | No clinically important laboratory abnormalities were noted | Cele [1] 3/73 Cele [2] 6/75 Cele [3] 7/73 Plac 2/70 No serious AEs drug-related | | | |
| C-020 OA 12 weeks | OA Knee/Hip (ACR) with flare FCC 1-3 Assessment at baseline, 2, 6, 12 weeks Washout 2-4 days Double dummy method Naprox QS 5/5; VS 16/16 | Cele [1] 2x50mg/day (n=218) Cele [2] 2x100mg/day (n=217) Cele [3] 2x200mg/day (n=222) Naprox 2x500mg/day (n=216) Plac (n=219) | Cele [1] 92/218 Cele [2] 91/217 Cele [3] 79/222 Naprox 85/216 Plac 121/219 | Cele [1] 67/218 Cele [2] 44/217 Cele [3] 52/222 Naprox 55/216 Plac 87/219 | Cele [1] 19/218 Cele [2] 35/217 Cele [3] 23/222 Naprox 18/216 Plac 17/219 GI-related: Cele [1] 3/218 Cele [2] 12/217 Cele [3] 7/222 Naprox 69/216 Plac 49/219 Cele [1] 12/218 Cele [2] 4/222 Naprox 3/216 Plac 4/219 Serious UGI: Cele [1] 0/218 Cele [2] 0/217 Cele [3] 0/222 Naprox 14/216 Plac 14/219 Diarrhoea: Cele [1] 12/218 Cele [2] 11/217 Cele [3] 15/222 Naprox 12/216 Plac 10/219 Vomiting: Cele [1] 2/218 Cele [2] 4/217 Cele [3] 4/222 Naprox 2/216 Plac 1/219 | Any: Cele [1] 150/218 Cele [2] 150/217 Cele [3] 144/222 Naprox 137/216 Plac 130/219 GI-related: Cele [1] 61/218 Cele [2] 58/217 Cele [3] 54/222 Naprox 69/216 Plac 49/219 Cele [1] 12/218 Cele [2] 8/217 Cele [3] 7/222 Naprox 14/216 Plac 14/219 Diarrhoea: Cele [1] 12/218 Cele [2] 11/217 Cele [3] 15/222 Naprox 12/216 Plac 10/219 Vomiting: Cele [1] 2/218 Cele [2] 4/217 Cele [3] 4/222 Naprox 2/216 Plac 1/219 | Duodenal ulcer: Cele [1] 1/218 Cele [2] 0/217 Cele [3] 0/222 Naprox 0/216 Plac 0/219 GIH: Cele [3] 19/222 Plac 0/219 Gastric ulcer: Cele [1] 0/218 Plac 0/219 | Mod/severe abdom pain, nausea, dyspepsia: Cele [1] 25/218 Cele [2] 16/217 Plac 0/219 GIH: Cele [3] 19/222 Plac 0/219 Gastric ulcer: Cele [1] 0/218 Plac 0/219 | Generalised Oedema: Cele [1] 1/218 Cele [2] 1/217 Cele [3] 1/222 Naprox 0/216 Plac 2/219 Aggravated hypertension: Cele [1] 0/218 Cele [2] 2/217 Cele [3] 4/222 Naprox 0/216 Plac 1/219 MI: Cele [1] 0/218 Cele [2] 0/217 Cele [3] 3/222 Naprox 0/216 Plac 0/219 Cardiac Failure: Cele [1] 1/218 Cele [2] 0/217 Cele [3] 0/222 Naprox 0/216 Plac 0/219 | Hypertension: Cele [1] 1/218 Cele [2] 3/217 Cele [3] 1/222 Naprox 0/216 Plac 2/219 Aggravated hypertension: Cele [1] 0/218 Cele [2] 2/217 Cele [3] 4/222 Naprox 0/216 Plac 1/219 MI: Cele [1] 0/218 Cele [2] 0/217 Cele [3] 3/222 Naprox 0/216 Plac 0/219 | Hct >5% decrease: Cele [1] 11/218 Cele [2] 13/217 Cele [3] 34/222 Naprox 25/216 Plac 21/219 No other clinically relevant lab results seen in more than 2% of patients in any group | Cele [1] 17/218 Cele [2] 21/217 Cele [3] 17/222 Naprox 15/216 Plac 12/219 | |

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| C-021 | OA Knee/Hip (ACR), with flare FCC 1-3 Assessment at baseline, 2, 6, 12 weeks Endoscopy at baseline, 12 weeks Washout 2-14 days Double dummy method QS 5/5; VS 16/16 | Cele [1] 16/258 Cele [2] 75/240 Cele [3] 79/237 Cele [2] 2x50mg/day (n=258) Cele [2] 2x100mg/day (n=239) Cele [3] 2x200mg/day (n=237) Naprox 2x500mg/day (n=233) Plac (n=247) | Cele [1] 86/258 Cele [2] 75/240 Cele [3] 79/237 Naprox 81/233 Plac 127/247 | Cele [1] 58/258 Cele [2] 51/239 Cele [3] 49/237 Naprox 41/233 Plac 92/247 | Cele [1] 16/258 Cele [2] 16/239 Cele [3] 23/237 Naprox 0/233 Plac 14/247 GI-related: Cele [1] 17/258 Cele [2] 10/239 Cele [3] 8/237 Naprox 18/233 Plac 5/247 | Any: Cele [1] 164/258 Cele [2] 157/239 Cele [3] 161/237 Cele [1] 14/247 GI-related: Cele [1] 17/258 Cele [2] 62/239 Cele [3] 74/237 Naprox 39/233 Plac 72/247 Serious: Cele [1] 1/258 Cele [2] 4/239 Cele [3] 7/237 Naprox 7/233 Plac 5/247 Serious UGI: Cele [1] 1/258 Cele [2] 2/239 Cele [3] 1/237 Naprox 1/233 Plac 1/247 Serious CV: Cele [1] 0/258 Cele [2] 2/239 Cele [3] 3/237 Naprox 1/233 Plac 3/247 | Dyspepsia: Cele [1] 24/258 Cele [2] 20/239 Cele [3] 29/237 Cele [1] 15/258 Cele [2] 11/239 Cele [3] 14/237 Naprox 18/233 Plac 9/247 | Duodenal ulcer: Cele [1] 0/258 Cele [2] 0/239 Cele [3] 0/237 Naprox 2/233 Plac 0/247 | Mod/severe abdominal pain, nausea, dyspepsia: Cele [1] 13/258 Cele [2] 18/239 Cele [3] 30/237 | Facial oedema: Cele [1] 0/258 Cele [2] 1/239 Cele [3] 1/237 | Cardiac Failure: Cele [1] 0/258 Cele [2] 0/239 Cele [3] 1/237 | Hct \geq 5% decrease: Cele [1] 23/258 Cele [2] 16/239 Cele [3] 21/237 | Cele [1] 23/258 Cele [2] 16/239 Cele [3] 21/237 Naprox 27/233 Plac 14/247 |
| C-042 | Symptomatic OA Hip/knee (ACR) at least 6 months, requiring NSAID FCC 1-3 Washout 2-5 days Assessment baseline, 2, 4, 6 weeks Double dummy method QS 5/5; VS 16/16 | Cele 200mg/day (n=348) Diclo 100mg/day (n=341) FCC 1-3 Washout 2-5 days Assessment baseline, 2, 4, 6 weeks Double dummy method QS 5/5; VS 16/16 | Cele 31/349 Diclo 40/341 | Cele 4/346 Diclo 3/341 | Cele 22/346 Diclo 29/341 GI-related: Cele 8/346 Diclo 16/341 Serious: Cele 3/346 Diclo 4/341 Serious UGI: None Serious CV: Cele 1/346 Diclo 1/341 | Any: Cele 150/346 Diclo 180/341 GI-related: Cele 59/346 Diclo 30/341 Serious: Cele 3/346 Diclo 4/341 Serious UGI: None Serious CV: Cele 1/346 Diclo 1/341 | Dyspepsia: Cele 11/346 Diclo 23/341 Abdom pain: Cele 17/346 Diclo 23/341 Nausea: Cele 11/346 Diclo 17/341 Diarrhoea: Cele 22/346 Diclo 26/341 Vomiting: Cele 4/346 Diclo 3/341 | Mod/severe abdominal pain, nausea, dyspepsia: Cele 11/346 Diclo 30/341 | Generalised oedema: Cele 1/346 Diclo 0/341 Peripheral oedema: Cele 7/346 Diclo 8/341 Hypertension: Cele 3/346 Diclo 0/341 Aggravated Hypertension: Cele 0/346 Diclo 4/341 | No clinically important laboratory abnormalities were noted | Cele 47/346 Diclo 62/341 | | |
| C-047 | OA Knee (ACR) with flare FCC 1-3 Washout NSAID 2 days, other 5 half-lives Assessment at baseline, 2, 4 weeks QS 5/5; VS 16/16 | Cele [1] 50mg/day (n=100) Cele [2] 200mg/day (n=101) Cele [3] 800mg/day (n=99) Plac (n=101) | Cele [1] 24/100 Cele [2] 22/101 Cele [3] 23/99 Plac 31/101 | Cele [1] 15/100 Cele [2] 13/101 Cele [3] 10/99 Plac 23/101 | Cele [1] 5/100 Cele [2] 4/101 Cele [3] 10/99 Plac 5/101 GI-related: Cele [1] 0/100 Cele [2] 1/101 Cele [3] 2/99 Plac 0/101 | Any: Cele [1] 61/100 Cele [2] 59/101 Cele [3] 56/99 Plac 5/101 GI-related: Cele [1] 0/100 Cele [2] 23/101 Cele [3] 19/99 Plac 9/101 Serious: Cele [1] 1/100 Cele [2] 2/101 Cele [3] 1/99 Plac 1/101 Serious UGI: Cele [1] 1/100 Cele [2] 0/101 Cele [3] 0/99 Plac 0/101 Serious CV: Cele [2] 1/101 Remaining =0 | Dyspepsia: Cele [1] 8/100 Cele [2] 9/101 Cele [3] 10/99 Plac 1/101 Abdom pain: Cele [1] 1/100 Cele [2] 0/101 Cele [3] 3/99 Plac 1/101 Nausea: Cele [1] 0/100 Cele [2] 5/101 Cele [3] 3/99 Plac 0/101 Diarrhoea: Cele [1] 10/100 Cele [2] 5/101 Cele [3] 3/99 Plac 2/101 Vomiting: Cele [1] 0/100 Cele [2] 1/101 Cele [3] 2/99 Plac 0/101 | Mod/severe abdominal pain, nausea, dyspepsia: Cele [1] 3/100 Cele [2] 7/101 Cele [3] 4/99 Plac 1/101 | Peripheral Oedema: Cele [1] 2/100 Cele [2] 1/101 Cele [3] 2/99 Plac 3/101 Aggravated hypertension: Cele [1] 0/100 Cele [2] 0/101 Cele [3] 2/99 Plac 0/101 | No clinically important laboratory abnormalities were noted | Cele [1] 1/100 Cele [2] 4/101 Cele [3] 12/99 Plac 3/101 | | |
| C-054 | OA Hip (ACR) with flare FCC 1-3 Washout 2-4 days Assessment at baseline, 2, 6, 12 weeks Double dummy method QS 5/5; VS 16/16 | Cele [1] 100mg/day (n=216) Cele [2] 200mg/day (n=213) Cele [3] 400mg/day (n=213) Naprox 1000mg/day (n=207) Plac (n=217) | Cele [1] 105/216 Cele [2] 96/207 Cele [3] 94/213 Naprox 89/207 Plac 138/217 | Cele [1] 76/216 Cele [2] 61/207 Cele [3] 55/213 Naprox 51/207 Plac 113/217 | Cele [1] 17/216 Cele [2] 27/207 Cele [3] 25/213 Naprox 29/207 Plac 16/217 GI-related: Cele [1] 6/216 Cele [2] 7/207 Cele [3] 11/213 Naprox 17/207 Plac 6/217 | Any: Cele [1] 125/216 Cele [2] 136/207 Cele [3] 131/213 Cele [1] 36/216 Cele [2] 39/207 Cele [3] 63/213 Naprox 73 Placbo 39/217 Serious: Cele [1] 3/216 Cele [2] 2/207 Cele [3] 3/213 Naprox 3/207 Plac 7/217 Serious UGI: Cele [1] 1/216 Cele [2] 1/207 Cele [3] 1/213 Naprox 1/207 Plac 3/217 | Dyspepsia: Cele [1] 8/216 Cele [2] 18/207 Cele [3] 21/213 Cele [1] 11/216 Cele [2] 10/213 Cele [3] 12/213 Placbo 39/217 Nausea: Cele [1] 8/216 Cele [2] 8/207 Cele [3] 12/213 Naprox 12/207 Placbo 52/217 Diarrhoea: Cele [1] 8/216 Cele [2] 13/207 Cele [3] 21/213 Naprox 11/207 Plac 12/217 | Vomiting: Cele [1] 2/216 Cele [2] 3/213 Cele [3] 3/213 Cele [1] 0/216 Cele [2] 0/207 Cele [3] 0/213 Plac 0/217 | Mod/severe abdominal pain, nausea, dyspepsia: Cele [1] 10/216 Cele [2] 13/207 Cele [3] 16/213 Naprox 20/207 Plac 10/217 | Generalised oedema: Cele [1] 0/216 Cele [2] 0/207 Cele [3] 1/213 Plac 0/217 | Aggravated hypertension: Cele [1] 0/216 Cele [2] 1/207 Cele [3] 1/213 Plac 0/207 | Hct \geq 5% decrease: Cele [1] 20/216 Cele [2] 9/213 Cele [3] 2/207 Plac 14/217 Hb \geq 20g/L decrease: Cele [1] 2/216 Cele [2] 0/207 Cele [3] 2/213 Plac 4/207 | Any: Cele [1] 11/216 Cele [2] 20/207 Cele [3] 17/213 Plac 9/217 |
| C-060 | OA Knee (ACR) with flare FCC 1-3 Washout NSAID 2 days, other 5 half-lives Assessment at baseline, 2, 6 weeks Double dummy method QS 5/5; VS 16/16 | Cele [1] 2x100mg/day (n=231) Cele [2] 1x200mg/day (n=222) Plac (n=231) | Cele [1] 37/231 Cele [2] 40/222 Plac 85/231 | Cele [1] 18/231 Cele [2] 21/222 Plac 56/231 | Cele [1] 11/231 Cele [2] 9/222 Plac 20/231 GI-related: Cele [1] 4/231 Cele [2] 3/222 Plac 9/231 Serious: Cele [1] 4/231 Cele [2] 0/222 Cele [3] 1/213 Naprox 1/207 Plac 3/217 | Any: Cele [1] 122/231 Cele [2] 111/222 Plac 120/231 GI-related: Cele [1] 40/231 Cele [2] 37/222 Plac 32/231 Serious: Cele [1] 4/231 Cele [2] 0/222 Cele [3] 1/213 Naprox 1/207 Plac 3/217 | Dyspepsia: Cele [1] 18/231 Cele [2] 12/222 Plac 10/231 Abdom pain: Cele [1] 4/231 Cele [2] 0/232 Placbo 7/231 Nausea: Cele [1] 5/231 Cele [2] 4/222 Placbo 12/231 Diarrhoea: Cele [1] 6/231 Cele [2] 10/222 Placbo 12/231 Vomiting: Cele [1] 1/231 Cele [2] 0/222 Placbo 1/231 | Mod/severe abdominal pain, nausea, dyspepsia: Cele [1] 4/231 Cele [2] 4/222 Plac 15/231 | Peripheral oedema: Cele [1] 1/231 Cele [2] 0/222 Plac 0/231 | Hct \geq 5% decrease: Cele [1] 13/231 Cele [2] 21/222 Plac 11/231 | Any: Cele [1] 8/231 Cele [2] 12/222 Plac 11/231 | | |
| C-087 | OA Knee (ACR) flare FCC 1-3 Washout 2 days for NSAID Assessed at baseline, 2, 6 weeks Double dummy method QS 5/5; VS 16/16 | Cele [1] 2x100mg/day (n=241) Cele [2] 1x200mg/day (n=231) Plac (n=243) | Cele [1] 47/243 Cele [2] 40/231 Plac 79/243 | Cele [1] 27/241 Cele [2] 24/231 Plac 55/243 | Cele [1] 9/241 Cele [2] 6/231 Plac 12/243 GI-related: Cele [1] 3/241 Cele [2] 0/231 Plac 3/243 Serious: Cele [1] 0/241 Cele [2] 2/231 Plac 1/243 Serious UGI: None reported Serious CV: Cele [1] 0/241 Cele [2] 1/231 Plac 0/243 | Any: Cele [1] 119/241 Cele [2] 124/231 Plac 116/243 GI-related: Cele [1] 49/241 Cele [2] 34/231 Plac 32/243 Serious: Cele [1] 0/241 Cele [2] 2/231 Plac 1/243 Serious UGI: None reported Serious CV: Cele [1] 0/241 Cele [2] 1/231 Plac 0/243 | Dyspepsia: Cele [1] 15/241 Cele [2] 9/231 Plac 12/243 Abdom Pain: Cele [1] 5/241 Cele [2] 2/231 Placbo 7/231 Nausea: Cele [1] 6/241 Cele [2] 7/231 Plac 7/231 Diarrhoea: Cele [1] 12/241 Cele [2] 7/231 Plac 3/243 Vomiting: Cele [1] 1/241 Cele [2] 1/231 Plac 1/243 | Mod/severe abdominal pain, nausea, dyspepsia: Cele [1] 9/241 Cele [2] 11/231 Plac 9/243 | Peripheral oedema: Cele [1] 6/241 Cele [2] 6/231 Plac 2/243 | Hct \geq 5% decrease: Cele [1] 3/241 Cele [2] 0/231 Cele [3] 4/231 Plac 1/243 | Any: Cele [1] 7/241 Cele [2] 12/231 Plac 11/243 | | |

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| C-096 12 weeks | OA (ACR) hip/knee/hand ≥6 months, requiring NSAID/analgesic, FCC 1-3 Double dummy method Assessed baseline, 6, 12 weeks AEs assessed by investigator examination and question and patient reported and laboratory test OS 5/5; VS 16/16 | Cele [1] 2x100mg/day (n=4393) Cele [2] 2x200mg/day (n=4407) Naprox 2x500mg/day (n=905) Diclo 2x50mg/day (n=3489) | Cele [1] 864/4393 Cele [2] 867/4407 Naprox 322/905 Diclo 530/3489 | Cele [1] 240/4393 Cele [2] 177/4407 Naprox 79/905 Diclo 97/3489 | Cele [1] 364/4393 Cele [2] 445/4407 Naprox 177/905 Diclo 274/3489 | Any AE: Cele [1] 1601/4393 Cele [2] 1673/4407 Diclo 1257/3489 GI-related: Cele [1] 206/4393 Cele [2] 254/4407 Naprox 134/905 Diclo 163/3489 | Dyspepsia: Cele [1] 1884/4393 Cele [2] 2344/4407 Diclo 1623/3489 Naprox 97/905 Abdom Pain: Cele [1] 203/4393 Cele [2] 220/4407 Diclo 193/3489 Naprox 81/905 Nausea: Cele [1] 100/4393 Cele [2] 107/4407 Diclo 82/3489 Naprox 69/905 Diarrhoea: Cele [1] 148/4393 Cele [2] 159/4407 Diclo 117/3489 Naprox 47/905 Vomiting: Cele [1] 25/4393 Cele [2] 22/4407 Diclo 29/3489 Naprox 22/905 | GIH: Cele [1] 2/4393 Cele [2] 1/4407 Diclo 1/3489 Naprox 1/905 Gastric ulcer: Cele [1] 1/4393 Cele [2] 1/4407 Gastric ulcer haemorrhagic: Cele [1] 0/4393 Cele [2] 2/4407 Diclo 1/3489 Naprox 2/905 Duodenal ulcer: Cele [1] 1/4393 Cele [2] 0/4407 Diclo 0/3489 Naprox 0/905 | Mod/severe abdom pain, nausea, dyspepsia: Cele [1] 209/4393 Cele [2] 225/4407 Diclo 200/3489 Naprox 130/905 | Generalised oedema: Cele [1] 33/4393 Cele [2] 9/4407 Diclo 8/3489 Naprox 8/905 Peripheral oedema: Cele [1] 69/4393 Cele [2] 80/4407 Diclo 28/3489 Naprox 35/905 Facial oedema: Cele [1] 10/4393 Cele [2] 11/4407 Diclo 8/3489 Naprox 1/905 | Hypertension: Cele [1] 41/4393 Cele [2] 53/4407 Diclo 44/3489 Naprox 11/905 Aggravated hypertension: Cele [1] 10/4393 Cele [2] 15/4407 Diclo 10/3489 Naprox 2/905 Cardiac Failure: Cele [1] 2/4393 Cele [2] 2/4407 Diclo 7/3489 Naprox 2/905 MI: Cele [1] 8/4393 Cele [2] 2/4407 Diclo 0/3489 Naprox 1/905 | Hb ≥20g/L decrease: Cele [1+2] 638/4407 Diclo+Naprox 31/2613 Hct ≥10% reduction: Cele [1+2] 8/6943 Diclo+Naprox 137/436 Creatinine ≥1.3xULN: Cele [1+2] 12/701 Diclo+Naprox (not all patients had haematological measurements) | Cele [1] 574/4393 Cele [2] 638/4407 Diclo 532/3489 Naprox 218/905 |
| C-118 6 weeks | OA knee (ACR) with flare, FCC 1-3 Washout 2 days for NSAIDs, other 5 half-lives Assessed at baseline, 2, 6 weeks OS 5/5; VS 16/16 | Cele 2x100mg/day (n=199) Diclo 3x50mg/day (n=199) Plac (n=200) | Cele 40/199 Diclo 37/199 Plac 71/200 | Cele 18/199 Diclo 10/199 Plac 42/200 | Cele 14/199 Diclo 22/199 Plac 14/200 | Any: Cele 99/199 Diclo 107/199 Plac 99/200 GI-related: Cele 35/199 Diclo 49/199 Plac 38/200 Serious: Cele 0/199 Diclo 4/199 Plac 1/200 GI-related: Cele 0/199 Diclo 0/199 Plac 1/200 Serious CV: Cele 0/199 Diclo 2/199 Plac 0/200 | Dyspepsia: Cele 11/199 Diclo 15/199 Plac 12/200 Abdom pain: Cele 7/199 Diclo 14/199 Plac 8/200 Nausea: Cele 4/199 Diclo 7/199 Plac 6/200 Diarrhoea: Cele 9/199 Diclo 13/199 Plac 10/200 Vomiting: Cele 1/199 Diclo 2/199 Plac 0/200 | Gastric ulcer: Cele 0/199 Diclo 1/199 Plac 0/200 | Mod/severe dyspepsia, abdom pain, nausea, dyspepsia: Cele 10/199 Diclo 13/199 Plac 10/200 | Generalised oedema: Cele 0/199 Diclo 1/199 Diclo 0/200 Peripheral oedema: Cele 10/199 Diclo 5/199 Placebo 1/200 Hypertension: Cele 1/199 Diclo 2/199 Placebo 0/200 Aggravated hypertension: Cele 0/199 Diclo 2/199 Placebo 1/200 | No report of MI or CHF | Hct ≥5% decrease: Cele 15/199 Diclo 23/199 Plac 17/200 Hb ≥20g/L decrease: Cele 1/199 Diclo 2/199 Plac 1/200 Creatinine ≥1.3xULN: Cele 1/199 Diclo 1/199 Placebo 1/200 | Any: Cele 16/199 Diclo 24/199 Plac 19/200 |
| C-149 6 weeks | OA Hand/Knee/Hip (ACR), requiring NSAID and/or analgesic, with treated stable hypertension FCC 1-3 Washout 4 days Double dummy method Assessment baseline, 1, 2, 6 weeks OS 5/5; VS 16/16 | Cele 1x200mg/day (n=411) Role 1x25mg/day (n=399) | Cele 64/411 Role 51/399 | Cele 8/411 Role 4/399 | All: Cele 37/411 Role 36/399 GI-related: Cele 11/411 (1 GI Bleed) GI Bleed) Role 10/399 GI related: Cele 67/411 Role 86/399 Serious UGI: Cele 2/411 Role 0/399 Possible others Any "renal event" (defined): Cele 123/411 Role 162/399 Composite renal event (defined): Cele 47/411 Role 72/399 | Excluding renal Any: Cele 237/411 Role 245/399 All Serious Cele 11/411 (1 GI Bleed) Role 10/399 GI related: Cele 67/411 Role 86/399 Serious UGI: Cele 2/411 Role 0/399 Possible others Any "renal event" (defined): Cele 123/411 Role 162/399 Composite renal event (defined): Cele 47/411 Role 72/399 | Dyspepsia: Cele 21/411 Role 29/399 Diarrhoea: Cele 17/411 Role 22/399 Abdom Pain: Cele 13/411 Role 20/399 Nausea: Cele 8/411 Role 11/399 Possible others frequency ≤2% | Mod/severe abdom pain, nausea, dyspepsia: Cele 13/411 Role 26/399 | Defined cardio-renal events: Cele 23/411 Role 26/399 Significant oedema: Cele 20/411 Role 38/399 Aggravated hypertension: Cele 23/411 Role 32/399 Composite renal events: Cele 47/411 Role 72/399 Secondary outcomes: Cele 123/411 Role 162/399 New/worsening oedema: Cele 78/411 Role 114/399 Elevated hypertension: Cele 58/411 Role 79/399 New/worsening CHF: Cele 9/411 Role 4/399 | Lab result: Cele 6/411 Role 6/399 Any renal event: Cele 123/411 Role 162/399 Hb ≥20g/L: Cele 0/411 Role 1/399 Not meeting above definitions: Peripheral oedema: Cele 5/411 Role 10/399 Hypertension: Cele 1/411 Role 0/399 Aggravated hypertension: Cele 1/411 Role 0/399 Cardiac Failure: Cele 0/411 Role 1/399 MI: Cele 1/411 Role 0/399 No clin relevant creatinine values reported | Lab test = renal event: Cele 6/411 Role 6/399 Hb ≥20g/L: Cele 0/411 Role 1/399 Hot ≥5% decrease: Cele 59/411 Role 76/399 No clin relevant creatinine values reported | Cele 27/411 Role 36/399 | |
| C-152 6 weeks | OA Knee (ACR) with flare, requiring NSAID ± analgesic, FCC 1-3 Washout ≥2days Double dummy method Assessed at baseline, 3, 6 weeks OS 5/5; VS 16/16 | Cele 1x200mg/day (n=63) Role 1x25mg/day (n=59) Plac (n=60) | Cele 14/63 Role 10/59 Plac 16/60 | Cele 5/63 Role 2/59 Plac 12/60 | All: Cele 4/63 Role 4/59 Plac 1/60 GI Related: Cele 1/63 Role 4/59 Plac 0/60 | Any AE: Cele 31/63 Role 36/59 Plac 2/60 GI-related: Cele 7/63 Role 20/59 Plac 6/60 Serious: Cele 1/63 Role 0/59 Plac 0/60 None | Dyspepsia: Cele 2/63 Role 6/59 Plac 4/60 Abdom Pain: Cele 1/63 Role 6/59 Plac 0/60 Nausea: Cele 1/63 Role 1/59 Plac 0/60 Diarrhoea: Cele 3/63 Role 4/59 Plac 0/60 Vomiting: Cele 1/63 Role 0/59 Plac 0/60 | Mod/severe abdom pain, nausea, dyspepsia: Cele 3/63 Role 5/59 Plac 0/60 | Peripheral oedema: Cele 2/63 Role 0/59 Plac 0/60 Aggravated hypertension: Cele 1/63 Role 1/59 Plac 1/60 | No report of MI or CHF | Hb ≥10g/L: Cele 3/63 Role 5/59 Plac 0/60 Creatinine ≥1.3xULN: None Ht ≥5% decrease: Cele 0/63 Plac 0/60 No withdrawals due to lab test results | All AEs: Cele 4/63 Role 6/59 Plac 0/60 No serious adverse event related to study medication | |
| C-181 6 weeks | OA (ACR) Hand/Knee/Hip, requiring NSAID or analgesic, with stable treated hypertension FCC 1-3 Washout 4 days Double dummy method Assessed at baseline, 1, 2, 6 weeks OS 5/5; VS 16/16 | Cele 1x200mg/day (n=549) Role 1x25mg/day (n=543) | Cele 51/549 Role 53/543 | Cele 4/549 Role 3/543 | All: Cele 26/549 Role 27/543 GI Related: Cele 11/549 Role 15/543 Cardio renal: Cele 8/549 Role 12/543 | Excluding cardio-renal Any AE: Cele 251/549 Role 248/543 Serious: Cele 12/549 Role 11/543 Cardiac failure 3) GI-related: Cele 83/549 Role 83/543 Cele 3/549 (Bleeds) Role 1/543 (Perforation) | Dyspepsia: Cele 24/549 Role 19/543 Abdom Pain: Cele 14/549 Role 22/543 Diarrhoea: Cele 21/549 Role 17/543 Any others occurred at frequency <2% | Mod/severe abdom pain, nausea, dyspepsia: Role 9/543 | Defined cardio-renal events: Cele 7/549 Role 12/543 Systolic BP: Cele 6.9% Role 14.9% Oedema: Cele 101/549 Role 136/543 Cardiac Failure: Cele 2/549 Role 3/543 | Not meeting above definitions: Oedema: Cele 26/549 Role 18/543 | Data not available | Data not available | |
| C-209 6 weeks | OA (ACR) knee with flare, requiring daily therapy, FCC 1-3 Double dummy method Assessed at baseline, 2, 6 weeks AEs observed or patient reported and laboratory tests OS 5/5; VS 16/16 | Cele 1x200mg/day (n=125) Naprox 2x500mg/day (n=66) | Cele 23/125 Naprox 18/125 Plac 22/66 | Cele 2/125 Naprox 2/125 Plac 0/66 | Cele 7/125 Naprox 7/125 Placebo 2/66 | Any AE: Cele 52/125 Naprox 51/125 Plac 35/66 GI-related: Cele 2/125 Naprox 6/125 Plac 4/66 Serious: Cele 1/125 Naprox 1/125 Plac 0/66 Serious UGI: Cele 0/125 Naprox 0/125 Plac 0/66 | Dyspepsia: Cele 11/125 Naprox 41/125 Plac 3/66 Abdom Pain: Cele 11/125 Naprox 3/125 Plac 3/66 Nausea: Cele 2/125 Naprox 3/125 Plac 2/66 Diarrhoea: Cele 3/125 Naprox 2/125 Plac 1/66 | Vomiting: ≤2% in any group | Mod/severe abdom pain, nausea, dyspepsia: Cele 0/125 Naprox 6/125 Plac 4/66 | oedema and hypertension: ≤2% in any group | Some "abnormal results" for Hb, Ht and creatinine due to lab test (Naprox) | Cele 32/125 Naprox 42/125 Plac 27/66 2 serious AEs were not treatment related | |

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| C-210 OA 6 weeks | OA Knee (ACR) with flare, requiring chronic NSAID/analgesic, FCC 1-3 Initial pain 40-100mm VAS Washout-2 days Assessed at baseline, 2, 6 weeks double-dummy method AEs observed by investigator and patient reported and laboratory tests QS 5/5; VS 16/16 | Cele 1x200mg/day (n=145) Naprox 2x500mg/day (n=141) Plac (n=76) | Cele 27/145 Naprox 39/141 Plac 19/76 | Cele 0/145 Naprox 0/141 Plac 5/76 | Cele 10/145 Naprox 15/141 Plac 3/76 | Any AE: Cele 40/145 Naprox 65/141 Plac 22/76 GI related: details not available Serious: No serious AEs Serious UGI: No serious UGI AEs | Dyspepsia: Cele 1% Naprox 4% Plac 0% Abdom pain: Cele 8% Naprox 12% Plac 4% Details of other outcomes not available | Mod/severe abdom pain, nausea, dyspepsia: Cele 5/145 Naprox 9/141 Plac 2/76 | oedema and hypertension in <2% in any treatment group | Abnormalities seen in Hct, Hb and creatinine No withdrawals | Cele 19/145 Naprox 34/141 Plac 6/76 Withdrawals: Cele 7/145 Naprox 13/141 Placebo 1/76 | | |
| C-211 OA 6 weeks | OA Knee with flare (X-ray confirmed) of NSAID requiring Initial pain 40-90 on 100mm VAS Washout >2 days Double dummy method Assessed at baseline, 2, 6 weeks AEs investigator observed and patient reported and laboratory tests QS 5/5; VS 16/16 | Cele 1x200mg/day (n=125) Naprox 2x500mg/day (n=129) Plac (n=61) | Cele 30/125 Naprox 36/129 Plac 16/61 | Cele 2/125 Naprox 3/129 Plac 5/61 | Cele 3/125 Naprox 9/129 Plac 1/61 | Any AE: Cele 46/125 Naprox 47/129 Plac 17/61 GI related: data not available Serious: Cele 0/125 Naprox 1/129 Placebo 0/61 Serious UGI: Cele 0/125 Naprox 1/129 (GI bleed) Plac 0/61 | Dyspepsia: Cele 4/125 Naprox 5/129 Plac 1/61 Abdom pain: Cele 2/125 Naprox 4/129 Plac 0/61 Details of other outcomes not available | Mod/severe abdom pain, nausea, dyspepsia: Cele 3/125 Naprox 4/129 Plac 1/61 | Not available | Not available | All AEs: Cele 17/125 Naprox 26/129 Plac 7/61 Withdrawals: Cele 2/125 Naprox 7/129 Plac 1/61 | | |
| C-216 OA 4 weeks | Symptomatic OA (X-ray confirmed) of NSAID requiring Initial pain ≥40 on 100 mm VAS Double dummy method Assessed at baseline, 2, 4 weeks AEs observed by investigator and laboratory tests QS 5/5; VS 16/16 | Cele 1x200mg/day (n=382) Loxo 3x600mg/day (n=385) Plac (n=192) | Cele 35/382 Naprox 36/385 Plac 15/192 | Cele 6/382 Loxo 3/385 Plac 4/192 | Cele 21/382 Loxo 24/385 Plac 7/192 | Any AE: Cele 203/382 Loxo 216/384 Plac 100/192 GI-related: Cele 104/382 Loxo 98/384 Plac 44/192 Serious: Cele 1/382 Loxo 3/384 Plac 1/192 Serious UGI: Cele 0/382 Loxo 0/384 Plac 0/192 | Dyspepsia: Cele 7/382 Loxo 7/384 Plac 4/192 Abdom Pain: Cele 35/382 Loxo 20/384 Plac 9/192 Nausea: Cele 6/382 Loxo 3/384 Plac 3/192 Diarrhoea: Cele 14/382 Loxo 19/384 Plac 5/192 Vomiting: Cele 1/382 Loxo 1/384 Plac 0/192 | Gastric ulcer: Cele 0/382 Loxo 2/384 Plac 0/192 Duodenal ulcer: Cele 0/382 Loxo 1/384 Plac 0/192 GIH: Cele 0/382 Loxo 2/384 (but not serious) Diarrhoea: Cele 14/382 Loxo 19/384 Plac 5/192 | Mod/severe abdom pain, nausea, dyspepsia: Cele 10/382 Loxo 9/384 Plac 3/192 | Generalised Oedema: Cele 0/382 Loxo 6/384 Plac 1/192 Periph Oedema: Cele 0/382 Loxo 4/384 Plac 0/192 Facial Oedema: Cele 2/382 Loxo 9/384 Plac 0/192 Hypertension: Cele 2/382 Loxo 2/384 Plac 0/192 Aggravated hypertension: Cele 0/382 Loxo 0/384 Plac 0/192 | Trial did not report any cases of heart failure Trial did not report any cases of MI Hct: essentially unchanged Hb: small changes, NS between groups Facial Oedema: Cele 0/184 Para 3/185 Facial Oedema: Cele 0/184 Para 1/185 No report of hypertension Aggravated hypertension: Cele 1/189 Para 1/185 Plac 0/182 Trial did not report any cases of heart failure Trial did not report any cases of MI | Hct: essentially unchanged Hb: small changes, NS between groups Facial Oedema: Cele 0/184 Para 1/185 No report of hypertension Aggravated hypertension: Cele 1/189 Para 1/185 Plac 0/182 Trial did not report any cases of heart failure Trial did not report any cases of MI | Cele 124/382 Loxo 152/384 Plac 60/192 No serious adverse events were related to the study medication Cele 0/192 Creatinine ≥300 micromol/L: Cele 4/363 Loxo 7/366 Plac 2/186 |
| C-249 OA 2x6 week crossover | OA Hip/Knee (K-L 2-4), requiring chronic NSAID/analgesic Initial pain 40-90 on 100mm (VAS) Washout between treatments 3-7 days Double dummy method Two periods each assessed at baseline and six weeks AEs investigator reported and laboratory tests QS 5/5; VS 16/16 | Cele 1x200mg/day (n=189) Para 64/185 Plac 69/182 Para 4x1000mg/day (n=185) Cele 17/146 Plac (n=182) (n2=91) | Period 1: Cele 36/189 Para 64/185 Plac 69/182 Para Cele 15/184 Para 10/146 Plac 20/91 | Period 1: Cele 20/189 Para 28/185 Plac 41/182 Period 2: Cele 6/184 Para 10/146 Plac 16/91 | Period 1: Para 8/185 Plac 7/182 GI-related: Cele 1/189 Para 4/185 Plac 0/182 Period 2: Cele 4/184 Para 4/146 Plac 1/91 | Period 1: Any AE: Cele 56/189 Para 57/185 Plac 30/182 GI-related: Cele 20/189 Para 21/185 Plac 13/182 Serious: Cele 1/189 Para 1/185 Plac 0/182 No serious UGI Period 2: Any AE: Cele 47/184 Para 30/146 Plac 15/184 Para 9/146 Plac 0/91 Serious: Cele 1/184 Para 0/146 Plac 0/91 No serious UGI | Period 1: Dyspepsia: Cele 3/189 Para 0/185 Plac 0/182 Abdom Pain: Cele 3/189 Para 0/185 Plac 0/182 Nausea: Cele 2/184 Para 1/146 Plac 0/91 Diarrhoea: Cele 3/189 Para 0/146 Plac 0/91 Vomiting: Cele 1/189 Para 0/146 Plac 0/91 | Period 2: Dyspepsia: Cele 3/184 Para 0/146 Plac 0/91 Abdom Pain: Cele 1/184 Para 0/146 Plac 0/91 Nausea: Cele 2/184 Para 1/146 Plac 0/91 Diarrhoea: Cele 3/184 Para 0/146 Plac 0/91 Vomiting: Cele 2/184 Para 0/146 Plac 0/91 | Period 1: Mod/severe abdom pain, nausea, dyspepsia: Cele 3/189 Para 3/185 Plac 0/182 Periods 1 and 2 combined: Mod/severe abdom pain, nausea, dyspepsia: Cele 5/373 Para 3/331 Plac 0/273 | Period 1: Generalised Oedema: Cele 0/189 Para 3/185 Facial Oedema: Cele 0/189 Para 1/185 Hypertension: Cele 0/189 Para 1/185 Plac 0/182 Aggravated hypertension: Cele 1/189 Para 1/185 Plac 0/182 Trial did not report any cases of heart failure Trial did not report any cases of MI | Period 2: Perip Oedema: Cele 4/184 Para 3/146 Plac 0/91 Facial Oedema: Cele 0/184 Para 1/146 Plac 0/91 Hypertension: Cele 1/189 Para 1/185 Plac 0/182 Aggravated hypertension: Cele 1/189 Para 1/185 Plac 0/182 Trial did not report any cases of heart failure Trial did not report any cases of MI | Hct: essentially unchanged Hb: small changes, NS between groups Facial Oedema: Cele 0/184 Para 1/146 Plac 0/91 No report of hypertension Aggravated hypertension: Cele 1/189 Para 1/185 Plac 0/182 Trial did not report any cases of heart failure Trial did not report any cases of MI | Period 1: data not provided Periods 1 and 2 combined: All AEs: Cele 26/373 Para 22/331 Placebo 14/273 |
| Rheumatoid arthritis | | | | | | | | | | | | | |
| C-012 RA 4 weeks | RA (ACR) (min 6 months) requiring NSAID FCC 1-3 Assessment at baseline, 1, 2, 4 weeks Double dummy method Washout 2 to 7 days QS 5/5; VS 16/16 | Cele [1] 2x40mg/day (n=80) Cele [2] 2x200mg/day (n=82) Cele [3] 2x400mg/day (n=81) Plac (n=84) | Cele [1] 18/80 Cele [2] 9/82 Cele [3] 10/81 Plac 25/84 | Cele [1] 14/80 Cele [2] 3/82 Cele [3] 5/81 Plac 15/84 | Cele [1] 3/80 Cele [2] 4/82 Cele [3] 4/81 Plac 5/84 | Any: Cele [1] 45/80 Cele [2] 48/82 Cele [3] 43/81 Plac 53/84 GI-related: Cele [1] 19/80 Cele [2] 16/82 Cele [3] 16/81 Plac 14/84 Serious: None No serious UGI No serious CV | Dyspepsia: Cele [1] 9/80 Cele [2] 8/82 Cele [3] 2/81 Plac 5/84 Abdom Pain: Cele [1] 4/80 Cele [2] 2/82 Cele [3] 2/81 Plac 4/84 Nausea: Cele [1] 3/80 Cele [2] 3/82 Cele [3] 4/81 Plac 5/84 Diarrhoea: Cele [1] 5/80 Cele [2] 4/82 Cele [3] 9/81 Plac 2/84 Vomiting: Cele [1] 1/80 Cele [2] 2/82 Cele [3] 1/81 Plac 0/84 | Mod/severe abdom pain, nausea, dyspepsia: Cele [1] 12/80 Cele [2] 5/82 Cele [3] 2/81 Plac 3/84 | Generalised oedema: Cele [1] 0/80 Cele [2] 0/80 Cele [3] 1/81 Plac 0/84 Peripheral hypertension: Cele [1] 2/80 Cele [2] 1/82 Cele [3] 2/81 Plac 0/84 Facial Oedema: Cele [1] 2/80 Cele [2] 2/82 Cele [3] 1/81 Plac 1/84 | Hypertension: Cele [1] 0/80 Cele [2] 1/80 Cele [3] 0/81 Plac 0/84 Aggravated hypertension: Cele [1] 0/80 Cele [2] 1/80 Cele [3] 0/81 Plac 0/84 | No clinically important laboratory abnormalities were noted | Cele [1] 9/80 Cele [2] 5/82 Cele [3] 8/81 Plac 6/84 | |
| C-022 RA 12 weeks | RA (ACR) (min 3 months) with flare, requiring NSAID FCC 1-3 Assessment at baseline, 2, 6, 12 weeks Endoscopy at 12 weeks Washout 2-7 days Double dummy method QS 5/5; VS16/16 | Cele [1] 2x100mg/day (n=240) Cele [2] 2x200mg/day (n=235) Cele [3] 2x400mg/day (n=218) Naprox 2x500mg/day (n=225) Placebo (n=231) | Cele [1] 86/240 Cele [2] 77/235 Cele [3] 81/218 Naprox 87/225 Plac 130/231 | Cele [1] 67/240 Cele [2] 50/235 Cele [3] 59/218 Naprox 65/225 Plac 104/231 | Cele [1] 13/240 Cele [2] 17/235 Cele [3] 12/218 Naprox 12/225 Plac 11/231 | Any: Cele [1] 164/240 Cele [2] 149/235 Cele [3] 135/217 Naprox 147/225 Plac 152/231 GI-related: Cele [1] 66/240 Cele [2] 59/235 Cele [3] 57/217 Naprox 69/225 Plac 45/231 Serious: Cele [1] 4/240 Cele [2] 4/235 Cele [3] 4/217 Plac 3/225 Plac 5/231 Serious UGI: Cele [1] 0/240 Cele [2] 0/235 Cele [3] 0/217 Naprox 1/225 Plac 0/231 Serious CV: Cele [1] 1/240 Cele [2] 2/235 Cele [3] 1/217 Naprox 0/225 Plac 2/231 | Dyspepsia: Cele [1] 24/240 Cele [2] 22/235 Cele [3] 22/217 Naprox 29/225 Plac 23/231 Abdom pain: Cele [1] 9/240 Cele [2] 9/235 Cele [3] 10/217 Naprox 15/225 Plac 0/231 Nausea: Cele [1] 10/240 Cele [2] 8/235 Cele [3] 7/217 Naprox 10/225 Plac 12/231 Diarrhoea: Cele [1] 13/240 Cele [2] 14/235 Cele [3] 15/217 Naprox 10/225 Plac 12/231 | Vomiting: Cele [1] 3/240 Cele [2] 2/235 Cele [3] 4/217 Naprox 3/225 Plac 2/231 Gastric Ulcer: Cele [1] 0/240 Cele [2] 1/235 Cele [3] 0/217 Naprox 1/225 Plac 0/231 | Mod/severe abdom pain, nausea, dyspepsia: Cele [1] 18/246 Cele [2] 17/235 Cele [3] 16/217 Plac 14/231 | Generalised Oedema: Cele [1] 1/240 Cele [2] 0/235 Cele [3] 1/217 Plac 0/231 Peripheral hypertension: Cele [1] 3/240 Cele [2] 3/235 Cele [3] 5/217 Naprox 4/225 Plac 0/231 Facial Oedema: Cele [1] 0/240 Cele [2] 1/235 Cele [3] 0/217 Plac 1/231 Hypertension: Cele [1] 0/240 Cele [2] 1/235 Cele [3] 2/217 Naprox 1/225 Plac 1/231 | MI: Cele [1] 0/240 Cele [2] 1/235 Cele [3] 0/217 Plac 0/231 Cardiac failure: no report of CF | Hct ≥5% decrease: Cele [1] 23/240 Cele [2] 29/235 Cele [3] 39/217 Plac 13/231 Hb ≥20g/L decrease: Cele [1] 1/240 Cele [2] 2/235 Cele [3] 4/217 Naprox 4/225 Plac 0/231 | Cele [1] 20/240 Cele [2] 23/235 Cele [3] 19/217 Plac 13/231 |

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| C-023 RA 12 weeks | RA (ACR) (min 3 months) with flare requiring NSAID FCC 1-3 Assessment at baseline, 2, 5, 12 weeks Washout 2-7 days Double dummy method. OS 5/5; VS 16/16 | Cele [1] 2x100mg/day (n=228) Cele [2] 2x200mg/day (n=218) Cele [3] 2x400mg/day (n=217) Naprox 2x500mg/day (n=218) Placebo (n=221) | Cele [1] 11/1/228 Cele [2] 94/218 Cele [3] 91/217 Naprox 85/218 Plac 143/221 | Cele [1] 92/228 Cele [2] 74/218 Cele [3] 69/217 Naprox 69/218 Plac 125/221 | Cele [1] 12/228 Cele [2] 16/218 Cele [3] 16/217 Naprox 16/218 Plac 12/221 | Any: Cele [1] 130/228 Cele [2] 126/218 Cele [3] 134/218 Naprox 133/218 Plac 114/221 GI-related: Cele [1] 52/228 Cele [2] 51/218 Cele [3] 52/217 Naprox 51/218 Plac 39/221 Serious: Cele [1] 2/228 Cele [2] 1/218 Cele [3] 2/217 Naprox 3/218 Plac 2/221 Serious UGI: Cele [1] 0/228 Cele [2] 0/218 Cele [3] 0/217 Naprox 1/218 Placebo 2/221 Serious CV: Cele [1] 1/228 Cele [2] 0/218 Cele [3] 2/217 Naprox 1/218 Plac 0/221 | Dyspepsia: Cele [1] 23/228 Cele [2] 18/218 Cele [3] 16/217 Naprox 29/218 Plac 13/221 Abdom pain: Cele [1] 10/228 Cele [2] 4/218 Cele [3] 5/217 Naprox 3/218 Plac 6/221 Nausea: Cele [1] 9/228 Cele [2] 7/218 Cele [3] 11/217 Naprox 8/218 Plac 11/221 | Diarrhoea: Cele [1] 13/228 Cele [2] 10/218 Cele [3] 13/217 Naprox 8/218 Plac 10/221 Vomiting: Cele [1] 1/228 Cele [2] 2/218 Cele [3] 7/217 Naprox 3/218 Plac 3/221 | Mod/severe abdom pain, nausea, dyspepsia: Cele [1] 17/228 Cele [2] 8/218 Cele [3] 11/217 Naprox 20/218 Plac 13/221 | Generalised oedema: Cele [1] 0/228 Cele [2] 0/218 Cele [3] 1/217 Naprox 0/218 Plac 1/221 Facial oedema: Cele [1] 3/228 Cele [2] 3/218 Cele [3] 6/217 Naprox 2/218 Plac 4/221 MI: Cele [1] 1/228 Cele [2] 0/218 Cele [3] 1/217 Naprox 0/218 Plac 0/221 Cardiac failure: Cele [1] 0/228 Cele [2] 0/218 Cele [3] 0/217 Naprox 1/218 Plac 0/221 | Hypertension: Cele [1] 0/228 Cele [2] 2/218 Cele [3] 1/217 Naprox 0/218 Plac 1/221 Aggravated hypertension: Cele [1] 1/228 Cele [2] 1/218 Cele [3] 1/217 Naprox 0/218 Plac 0/221 Cardiac failure: Cele [1] 0/228 Cele [2] 0/218 Cele [3] 0/217 Naprox 1/218 Plac 0/221 | Hct <5% decrease: Cele [1] 15/228 Cele [2] 15/218 Cele [3] 21/217 Naprox 16/218 Plac 11/221 Hb >20g/L decrease: less than 1% of patients | Cele [1] 17/228 Cele [2] 12/218 Cele [3] 20/217 Naprox 24/218 Plac 15/221 |
| C-041 RA 6 months | RA (ACR) (min 6 months) requiring NSAID FCC 1-3 Assessment at baseline, weeks, 4, 8, 12, 16, 20 and 24 weeks Endoscopy 24 weeks Washout* - no investig drug <30days Double dummy method OS 5/5; VS 16/16 | Cele 2x200mg/day (n=326) Diclo SR 2x75mg/day (n=329) | Cele 68/326 Diclo 94/329 | Cele 26/326 Diclo 22/329 | Cele 34/326 Diclo 64/329 | Any: Cele 222/326 Diclo 239/329 GI-related: Cele 118/326 Diclo 159/329 Serious: Cele 14/326 Diclo 16/329 Serious UGI: Cele 0/326 Diclo 5/329 Serious CV: Cele 1/326 Diclo 1/329 | Dyspepsia: Cele 34/326 Diclo 42/329 Abdom pain: Cele 36/326 Diclo 68/329 Nausea: Cele 15/326 Diclo 27/329 Diarrhoea: Cele 39/326 Diclo 46/329 Vomiting: Cele 0/326 Diclo 17/329 | Duodenal ulcer: Cele 2/269 Naprox 2/267 Gastric ulcer: Cele 0/326 Diclo 9/329 Haemorrhagic Gastritis: Cele 0/326 Diclo 1/329 | Mod/severe abdom pain, nausea, dyspepsia: Cele 31/326 Diclo 77/329 | Generalised oedema: Cele 0/326 Diclo 2/329 Peripheral oedema: Cele 11/326 Diclo 5/329 Facial oedema: Cele 1/326 Diclo 2/329 Hypertension: Cele 4/326 Diclo 5/329 MI: Cele 1/326 Diclo 0/329 Cardiac failure: Cele 2/326 Diclo 1/329 | Hct <5% decrease: Cele 35/329 Cele 25/326 Diclo 57/329 Hb >20g/L decrease: Cele 14/326 Diclo 18/329 Creatinine >1.3xULN: Cele 4/326 Diclo 2/329 | Cele 74/326 Diclo 97/329 | |
| C-062 OA/RA 12 weeks | OA/RA (ACR) (min 3 months) with flare FCC 1-3 Assessed (including endoscopy) at baseline, 4, 8, 12 weeks Washout >30 days for naprox OS 5/5; VS 16/16 | Cele 2x200mg/day (n=269) Diclo 2x75mg/day (n=267) | Cele 59/269 Naprox 118/267 | Cele 17/269 Diclo 10/387 Ibu 14/345 | Cele 19/269 Naprox 24/267 Ibu 37/345 GI-related: Cele 11/269 Diclo 16/267 plus endoscopic ulcer: Cele 12/269 Ibu 6/267 Serious UGI: Cele 1/269 Naprox 1/267 Serious CV: Cele 2/269 Naprox 4/267 | Dyspepsia: Cele 34/269 Naprox 29/267 Abdom Pain: Cele 23/269 Diclo 33/267 GI-related: Cele 9/269 Naprox 23/267 Diarrhoea: Cele 11/269 Naprox 17/267 Vomiting: Cele 0/269 Naprox 4/267 | Duodenal ulcer: Cele 2/269 Naprox 2/267 Gastric ulcer: Cele 1/269 Naprox 1/267 Haemorrhagic Gastritis: Cele 1/269 Naprox 1/267 Peptic ulcer: Cele 0/269 Naprox 1/267 | Mod/severe abdom pain, nausea, dyspepsia: Cele 20/269 Naprox 35/267 | Peripheral oedema: Cele 8/269 Naprox 8/267 Hypertension: Cele 5/269 Naprox 3/267 Aggravated hypertension: Cele 1/269 Naprox 1/267 Anasemia: Cele 0/269 Naprox 4/267 | MI: Cele 1/269 Naprox 1/267 No report of CHF Hypertension: Cele 2/365 Diclo 0/387 Cele 0/345 Cardiac Failure: Cele 1/365 Diclo 0/387 Ibu 0/345 Generalised oedema: Cele 0/365 Diclo 0/387 Ibu 1/345 Hypertension: Cele 5/365 Diclo 2/387 Ibu 2/345 | Hct <5% decrease: Cele 77/365 Diclo 103/387 Hb >20g/L: Cele 6/269 Naprox 7/267 Creatinine >1.3xULN: Cele 3/269 Naprox 1/267 No lab findings considered clinically sig and no pattern suggesting any changes due to drug-related process | Cele 29/269 Naprox 49/267 Ibu 52/345 | |
| C-071 OA/RA 12 weeks | OA/RA (ACR) (min 3 months) requiring NSAID FCC 1-3 Assessed (including endoscopy) at baseline, 4, 8, 12 weeks Washout >30 days for chronic diclo or ibu OS 5/5; VS 16/16 | Cele 2x200mg/day (n=365) Diclo 2x75mg/day (n=387) Ibu 3x800mg/day (n=345) | Cele 77/365 Diclo 99/387 Ibu 115/345 | Cele 18/365 Diclo 10/387 Ibu 14/345 | Cele 22/365 Diclo 37/387 Ibu 37/345 GI-related: Cele 11/365 Diclo 22/387 Ibu 26/345 plus endoscopic ulcers: Cele 19/365 Diclo 27/387 Ibu 47/345 Serious UGI: Cele 1/365 (GH) Ibu 0/345 | Dyspepsia: Cele 34/365 Diclo 42/387 Ibu 44/345 Abdom Pain: Cele 22/365 Diclo 35/387 Ibu 41/345 Nausea: Cele 12/365 Diclo 13/387 Ibu 23/345 Diarrhoea: Cele 20/365 Diclo 36/387 Ibu 20/345 | Vomiting: Cele 5/365 Diclo 8/387 Ibu 6/345 Gastric ulcer: Cele 0/365 Diclo 0/387 Ibu 1/345 Haemorrhagic: Cele 1/365 Diclo 0/387 Ibu 1/345 | Mod/severe abdom pain, nausea, dyspepsia: Cele 33/365 Diclo 49/387 Ibu 40/345 | Peripheral oedema: Cele 6/365 Diclo 4/387 Ibu 12/345 Facial oedema: Cele 1/365 Diclo 1/387 Ibu 2/345 Generalised oedema: Cele 0/365 Diclo 1/387 Ibu 0/345 Hypertension: Cele 5/365 Diclo 2/387 Ibu 2/345 | Aggravated hypertension: Cele 2/365 Diclo 0/387 Ibu 0/345 Cardiac Failure: Cele 0/365 Diclo 0/387 Ibu 1/345 MI: Cele 0/365 Diclo 0/387 Ibu 0/345 Generalised oedema: Cele 0/365 Diclo 0/387 Ibu 1/345 Hypertension: Cele 5/365 Diclo 2/387 Ibu 2/345 | Hct <5% decrease: Cele 77/365 Diclo 103/387 Hb >20g/L: Cele 15/345 Ibu 15/345 Creatinine >1.3xULN: Cele 4/387 Ibu 8/345 No lab findings considered clinically sig and no pattern suggesting any changes due to drug-related process | Cele 28/365 Diclo 49/387 Ibu 52/345 | |
| C-102 OA/RA 52 weeks | OA/RA (documented) (min 3 months) requiring NSAID FCC 1-3 Assessed at baseline 13, 26, 39, 52 weeks Washout 30 days OS 5/5; VS 16/16 | Cele 2x400mg/day (n=388) Ibu 3x800 mg/day (n=1985) Diclo 2x75mg/day (n=1996) OS 5/5; VS 16/16 | Cele 2208/3987 Ibu 1294/1985 Diclo 1057/1996 | Cele 2208/3987 Ibu 1294/1985 Diclo 1057/1996 | Any: Cele 892/3987 Ibu 456/1985 Diclo 529/1996 GI-related: Cele 1819/3987 Ibu 917/1985 Cele 1097/1996 Diclo 270/3987 Ibu 119/1985 Diclo 111/1996 Serious UGI: Cele 4/3987 Ibu 19/1985 Diclo 23/1996 | Dyspepsia: Cele 659/3987 Ibu 328/1985 Diclo 390/1996 Abdom Pain: Cele 466/3987 Ibu 225/1985 Diclo 370/1996 Nausea: Cele 329/3987 Ibu 178/1985 Diclo 242/1996 Diarrhoea: Cele 434/3987 Ibu 148/1985 Diclo 299/1996 Vomiting: Cele 103/3987 Ibu 53/1985 Diclo 69/1996 | Duodenal Ulcer: Cele 17/3987 Ibu 6/1985 Diclo 8/1996 Duodenal bleeding: Cele 0/3987 Ibu 1/1985 Gastric Ulcer: Cele 21/3987 Ibu 25/1985 Diclo 16/1996 Gastric bleeding: Cele 5/3987 Ibu 2/1985 Diclo 0/1996 GIH: Cele 9/3987 Ibu 2/1985 Diclo 2/1996 | Clin sig UGI event (Trad definition) Cele 20/3987 Ibu 13/1985 Diclo 11/1996 | Generalised Oedema: Cele 19/3987 Ibu 20/1985 Diclo 11/1996 Peripheral Oedema: Cele 14/3987 Ibu 104/1985 Diclo 70/1996 Facial Oedema: Cele 21/3987 Ibu 8/1985 Diclo 4/1996 Aggravated Hypertension: Cele 78/3987 Ibu 61/1985 Diclo 40/1996 Hypertension: Cele 32/3987 Ibu 24/1985 Diclo 12/1996 | Cardiac Failure: Cele 12/3987 Ibu 9/1985 Diclo 3/1996 MI: Cele 19/3987 Ibu 9/1985 Diclo 5/1996 Facial Oedema: Cele 21/3987 Ibu 8/1985 Diclo 4/1996 Hypertension: Cele 78/3987 Ibu 61/1985 Diclo 40/1996 Aggravated Hypertension: Cele 32/3987 Ibu 24/1985 Diclo 12/1996 | Hct <5% decrease: Cele 12/3987 Ibu 4/3701 Diclo 2/1802 MI: Cele 5/1849 Hb <8 or 30g/L decrease: Cele 9/3708 Ibu 7/1905 Diclo 9/1851 Creatinine >300 ULN: Cele 67/3967 Ibu 271/759 Diclo 33/1840 | Cele 18/327 Diclo 20/330 | |
| C-105 OA/RA 12 weeks | OA/RA (Documented >3 months) requiring NSAID FCC 1-3 Assessment at baseline, 4, 8, 12 weeks Endoscopy at baseline, 12 weeks Double dummy method Washout >30 days for diclo OS 5/5; VS 16/16 | Cele 2x100mg/day (n=327) Diclo 2x50mg/day (n=330) | Cele 37/327 Diclo 40/330 | Cele 11/327 Diclo 7/330 | Cele 12/327 Diclo 18/330 GI-related: Cele 7/327 Diclo 14/330 Serious: Cele 2/327 Diclo 4/330 Serious GI: Cele 2/327 Diclo 1/330 | Dyspepsia: Cele 9/327 Diclo 16/330 Abdom Pain: Cele 43/327 Diclo 62/330 Nausea: Cele 8/327 Diclo 12/330 Diarrhoea: Cele 6/327 Diclo 5/330 Vomiting: Cele 6/327 Diclo 5/330 | Gastric ulcer: Cele 0/327 Diclo 2/330 dyspepsia: Cele 0/327 Diclo 2/330 Duodenal ulcer: Cele 0/327 Diclo 1/330 | Mod/severe abdom pain, nausea, dyspepsia: Cele 20/327 Diclo 30/330 | Peripheral oedema: Cele 2/327 Diclo 3/330 Facial oedema: Cele 4/327 Diclo 1/330 Oedema: Cele 0/327 Diclo 3/330 Hypertension: Cele 7/327 Diclo 12/330 | Hct <5%decrease: Cele 30/327 Diclo 31/330 Hb >20g/L decrease: Cele 32/327 Diclo 40/330 Creatinine >1.3xULN: Cele 1/327 Diclo 0/330 | Cele 18/327 Diclo 20/330 | | |

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| C-106 | OA/RA (Documented), requiring NSAID FCC 1-3 Assessment at baseline, 4, 8, 12 weeks Endoscopy at baseline and 12 weeks Double dummy method Washout ≥30 days for dico | Cele 2x100mg/day (n=63) Dico 2x50mg/day (n=61) | Cele 7/63 Dico 11/61 | Cele 1/63 Dico 4/61 | Cele 1/63 Dico 4/61 GI-related: Cele 0/63 Dico 3/61 | Any: Cele 28/63 GI-related: Cele 9/63 Dico 17/61 Serious: Cele 2/63 Dico 1/61 Serious UGI: Cele 0/63 Dico 0/61 | Dyspepsia: None reported Abdom Pain: Cele 0/63 Dico 1/61 Nausea: Cele 2/63 Dico 1/61 Diarrhoea: Cele 2/63 Dico 3/61 Vomiting: None reported | Haemorrhagic gastric ulcer: Cele 0/63 Dico 1/61 | Mod/severe abdom pain, nausea, dyspepsia: Cele 0/63 Dico 2/61 "Mod/severe GI related": Cele 0/63 Dico 6/61 | Facial oedema: Cele 2/63 Dico 0/61 Peripheral oedema: Cele 0/63 Dico 3/61 No reports of hypertension or CHF ??MI | Hct ≥5% decrease: Cele 2/63 Dico 2/61 Hb ≥20 g/L decrease: Cele 0/63 Dico 0/61 Creatinine ≥1.3xULN: Cele 0/63 Dico 0/61 | Cele 2/63 Dico 2/61 |
| | QS 5/5; VS 16/16 | | | | | | | | | | | |
| C-107 | OA/RA (Documented ≥3 months), requiring NSAID, FC 1-3 Assessment at baseline, 4, 8, 12 weeks Endoscopy at baseline, 12 weeks Double dummy method Washout ≥30 days for dico | Cele 2x100mg/day (n=44) Dico 2x50mg/day (n=44) | Cele 6/44 Dico 9/44 | Cele 1/44 Dico 2/44 | Cele 2/44 Dico 5/44 GI-related: Cele 2/44 Dico 3/44 Serious: Cele 2/44 Dico 11/44 Serious UGI: Cele 1/44 Dico 0/44 Serious CV: Cele 1/44 Dico 1/44 | Any: Cele 28/44 Dico 32/44 GI-related: Cele 13/44 Dico 11/44 Serious: Cele 2/44 Dico 4/44 Diarrhoea: Cele 1/44 Dico 0/44 Vomiting: Cele 4/44 Dico 1/44 | Dyspepsia: Cele 0/44 Dico 5/44 Abdom pain: Cele 13/44 Dico 3/44 Nausea: Cele 2/44 Dico 1/44 Diarrhoea: Cele 2/44 Dico 2/44 | Mod/severe abdom pain, nausea, dyspepsia: Cele 7/44 Dico 6/44 | Facial oedema: Cele 0/44 Dico 1/44 Hypertension: Cele 1/44 Dico 1/44 No report of MI or CHF | Week 12 Hct ≥5% decrease: Cele 1/44 Dico 0/44 Hb ≥20g/L decrease: None Creatinine ≥1.3xULN: None | Cele 7/44 Dico 13/44 | |
| | QS 5/5; VS 16/16 | | | | | | | | | | | |

Abdom = abdominal; ACR = American College of Rheumatology; AE = adverse event; BP = blood pressure; Cele = celecoxib; CF = cardiac failure; CHF = chronic heart failure; Clin = clinically; CV = cardiovascular; Dico = diclofenac; GI = gastrointestinal; GIH = gastrointestinal haemorrhage; GIH = gastrointestinal haemorrhage; Hct = haematocrit; Ibu = ibuprofen; K-L = Kellgren-Lawrence; Loxo = loxoprofen; MI = myocardial infarction; Mod = moderate; Naprox, Nap = naproxen; NSAID = nonsteroidal anti-inflammatory drug; OA = osteoarthritis; Para = paracetamol; Para = paracetamol; periph = peripheral; Plac = placebo; QS = quality score; Rofe = rofecoxib; sig = significant; Trad = traditional; UGI = upper gastrointestinal; VAS = visual analogue scale; VS = validity score.