

Additional file 1: Details of trials and information extracted on discontinuations

Trial number	Description	Demographics	Duration weeks Compliance Exposure	Treatments (N)	All cause	Lack of efficacy	Clinical AE
Studies of 4-6 weeks							
805	OA knee or hip At least 40 years Radiographic diagnosis At least 6/12 symptoms Minimum 40/100 mm at inclusion on flare visit, plus ≥15 mm increase and worsening in investigator global assessment since baseline visit	Female 80% Caucasian 81% Mean age 63 years Age range 38-89 years Hip 23% Knee 77% Median duration 5 years ARA Class II/III 80%	6 E60 40 Diclo 150 41	E60 256 Diclo 150 260	E 27 Diclo 15	E 7 Diclo 1	E 14 Diclo 9
806	Chronic low back pain At least 18 years Use of analgesics or NSAID regularly 30 days. Minimum 40/100 mm at inclusion washout visit, plus increase of ≥10 mm, and worsening in investigator assessment since	Female 72% Caucasian 74% Mean age 52 years Age range <20-90 years	4 E 60 27 Diclo 150 27	E 60 224 Diclo 150 222	E 20 Diclo 25	E 1 Diclo 5	E 15 Diclo 13
007	OA knee At least 40 years Radiographic and clinical diagnosis At least 6/12 symptoms Minimum 40/100 mm at inclusion on flare visit, plus ≥15 mm increase and worsening in investigator global assessment since baseline visit	Female 72% White 89% Mean age 61 years Age range 40-87 years Median duration 6 years ARA Class II/III 85%	6 E 5 41 E10 39 E30 42 E60 41 E90 42 Pbo 38	E 5 117 E10 114 E30 102 E60 112 E90 112 Pbo 60	E 5 12 E10 17 E30 8 E60 9 E90 11 Pbo 10	E 5 6 E10 11 E30 4 E60 2 E90 2 Pbo 7	E 5 2 E10 2 E30 3 E60 3 E90 6 Pbo 2
32	At least 18 years Diagnosis of AS by NY criteria At least 6/12 symptoms Minimum 40/100 mm at inclusion flare visit	Female 22% White 71% Mean age 44 years Age range 18-78 years	6 E90 41 E120 41 Nap 1000 39 Pbo 31	E90 103 E120 92 Nap 1000 99 Pbo 93	E90 11 E120 9 Nap 1000 21 Pbo 45	E90 8 E120 9 Nap 1000 20 Pbo 44	E90 2 E120 0 Nap 1000 1 Pbo 0

Studies of 8-12 weeks

010	At least 4 of 7 ARA criteria	Female 83%	8	E10 78	E10 11	E10 5	E10 2
	At least 6/12 duration	White 62%, Hispanic 27%	E10 52	E60 126	E60 9	E60 2	E60 6
	18 years or older	Mean age 52 years	E60 54	E90 134	E90 6	E90 2	E90 3
	Patient global assessment \geq 40 mm, \geq 9 tender and \geq 6 swollen joints	Age range 16 to 82 years	E90 55	E120 120	E120 10	E120 3	E120 5
		Median duration 7 years ARA Class II/III 71% methotrexate 31%, corticosteroid 22%	E120 53 Pbo 53	Pbo 123	Pbo 15	Pbo 11	Pbo 3
018	OA knee or hip	Female 66%	12	E60 222	E60 37	E60 13	E60 17
	At least 40 years	White 91%	E60 78	Nap1000 218	N1000 35	N1000 9	N1000 19
	Radiographic diagnosis	Mean age 62 years	Nap1000 77	Pbo 56	Pbo 18	Pbo 11	Pbo 3
	At least 6/12 symptoms	Age range 40 to 92 years	Pbo 69				
	Minimum 40/100 mm at inclusion on flare visit, plus \geq 15 mm increase and worsening in investigator global assessment since baseline visit	Hip 19% Knee 81% Median duration 5 years ARA Class II/III 76%					
019	OA knee or hip	Female 78%	12	E60 224	E60 20	E60 7	E60 5
	At least 40 years	White 72%	E60 81	Nap1000 221	N1000 37	N1000 7	N1000 24
	Radiographic diagnosis	Mean age 63 years	Nap1000 77	Pbo 56	Pbo 12	Pbo 6	Pbo 6
	At least 6/12 symptoms	Age range 35 to 84 years	Pbo 73				
	Minimum 40/100 mm at inclusion on flare visit, plus \geq 15 mm increase and worsening in investigator global assessment since baseline visit	Hip 25% Knee 75% Median duration 4 years ARA Class II/III 81%					
024	At least 4 of 7 ARA criteria	Female 77%	12	E90 323	E90 93	E90 70	E90 11
	At least 6/12 duration	White 87%	E90 70	Nap1000 170	Nap1000 71	Nap1000	Nap1000
	18 years or older	Mean age 56 years	Nap1000 62	Pbo 323	Pbo 201	62	13
	Patient global assessment \geq 40 mm, \geq 6 tender and \geq 2 swollen joints	Age range 21 to 99 years	Pbo 48			Pbo 176	Pbo 8
		Median duration 6.7 years ARA Class II/III 79% methotrexate 48%, corticosteroid 32%					

025	At least 4 of 7 ARA criteria At least 6/12 duration 18 years or older Patient global assessment \geq 40 mm, \geq 6 tender and \geq 2 swollen joints	Female 77% White 87% Mean age 56 years Age range 21 to 99 years Median duration 6.7 years ARA Class II/III 79% methotrexate 48%, corticosteroid 32%	12 E90 76 Nap1000 77 Pbo 66	E90 353 Nap1000 181 Pbo 357	E90 59 Nap1000 30 Pbo 115	E90 44 Nap1000 19 Pbo 90	E90 9 Nap1000 5 Pbo 6
026	OA or RA needing NSAID for at least 3 months RA 18 years or older Diagnosis at least 6/12 OA 50 years or older	Female 82% White 57%, Hispanic 20% Mean age 54 years Age range 18 to 83 years OA 25%, RA 75%	12 E120 74 Nap1000 69 Pbo 75	E120 251 Nap1000 244 Pbo 247	E120 51 Nap1000 94 Pbo 42	E120 6 Nap1000 3 Pbo 14	E120 16 Nap1000 25 Pbo 14
029	Established OA needing NSAID for at least 3 months At least 50 years	Female 74% White 80% Mean age 62 years Age range 45 to 99 years	12 E120 76 Ibu 2400 73 Pbo 77	E120 221 Ibu 2400 226 Pbo 233	E120 40 Ibu 2400 66 Pbo 40	E120 2 Ibu 2400 3 Pbo 6	E120 17 Ibu 2400 15 Pbo 11
041	Age 18 to 75 years Mnimum 40 /100 mm at randomisation, $>$ 10 mm since screen, worsening since screen	Female 63% White 92% Mean age 53 years Age range 19 to 78 years	12 E60 70 E90 70 Pbo 68	E60 109 E90 106 Pbo 110	E60 32 E90 29 Pbo 33	E60 9 E90 7 Pbo 17	E60 12 E90 11 Pbo 7

042	Age 18 to 75 years Mnimum 40 /100 mm at randomisation, >10 mm since screen, worsening since screen	Female 61% White 89% Mean age 52 years Age range 20 to 75 years	12 E60 71 E90 67 Pbo 64	E60 103 E90 107 Pbo 109	E60 28 E90 35 Pbo 44	E60 6 E90 12 Pbo 27	E60 12 E90 12 Pbo 9
065	Age 40 years or more Diagnosis of OA treated with NSAID/coxib	Female 60% White 80% Age range 40 to over 80 years, mean about 60 years	12 Drug exposure close to 100% E90 72 Cel 400 73 Ibu 2400 72 Pbo 68	E90 108 Cel 400 107 Ibu 2400 107 Pbo 111	E90 25 Cel 400 23 Ibu 2400 24 Pbo 32	E90 5 Cel 400 3 Ibu 2400 4 Pbo 13	E90 12 Cel 400 11 Ibu 2400 Pbo 9
071	OA knee or hip Clinical and radiographic criteria At least 6/12 symptoms Minimum 40/100 mm pain, increase of at least 15 mm from baseline, and worsening since baseline	Female 71% White 89% Mean age 62 years Age range 40 to 89 years	12 Compliance 94% Mean days on drug E30 75 Ibu 2400 67 Pbo 56	E30 214 Ibu 2400 210 Pbo 104	E30 42 Ibu 2400 64 Pbo 49	E30 25 Ibu 2400 30 Pbo 31	E30 11 Ibu 2400 22 Pbo 6
073	OA knee or hip Clinical and radiographic criteria At least 6/12 symptoms Minimum 40/100 mm pain, increase of at least 15 mm from baseline, and worsening since baseline	Female 76% White 48% Mean age 63 years Age range 41 to 86 years	12 Compliance 93% Mean days on drug E30 74 Ibu 2400 71 Pbo 66	E30 224 Ibu 2400 213 Pbo 221	E30 41 Ibu 2400 46 Pbo 32	E30 16 Ibu 2400 15 Pbo 21	E30 11 Ibu 2400 19 Pbo 5
076	OA knee or hip Clinical and radiographic criteria At least 6/12 symptoms Minimum 40/100 mm pain, increase of at least 15 mm from baseline, and worsening since baseline	Female 67% White 88% Mean age 62 years Age range 40 to 91 years ARA II/III 82%	12 Compliance 99% Mean days on drug E30 78 C200 73 Pbo 67	E30 231 C200 241 Pbo 127	E30 40 C200 49 Pbo 42	E30 14 C200 22 Pbo 31	E30 10 C200 12 Pbo 6

077	OA knee or hip Clinical and radiographic criteria At least 6/12 symptoms Minimum 40/100 mm pain, increase of at least 15 mm from baseline, and worsening since baseline	Female 66% White 88% Mean age 62 years Age range 41 to 88 years ARA II/III 79%	12 Compliance 99% Mean days on drug E30 79 C200 76 Pbo 56	E30 244 C200 247 Pbo 117	E30 32 C200 45 Pbo 57	E30 15 C200 24 Pbo 39	E30 7 C200 8 Pbo 12
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Studies of >24 weeks

061	OA knee, hip, hand, spine Age at least 5 years NSAID needed for 12 months	Female 72% White 85% Mean age 64 years Age range 44 to 92	52 E90 9.3 Dic 150 8.9 E90 2789 py Dic 150 2604 py	E90 3593 Dic 150 3518	E90 1455 Dic 150 1612	E90 350 Dic 150 374	E90 632 Dic 150 610
066	At least 50 years OA of knee, hip, hand, or spine or RA (4 of 7 ARA criteria)	Female 74% White 79% Mean age 63 years Age range 45 to 94 years	52+ OA E60 20.8 m/11746 py D150 20.2 mo/11288 py OA E90 20.4 mo/3686 py D150 19.4 mo/3491 py RA E90 20.8 mo/4917 py D150 20.1 mo/4786 py	OA E60 6769 D150 6700 OA E90 2171 D150 2162 RA E90 2841 D150 2855	OA E60 3524 D150 3590 OA E90 1584 D150 1582 RA E90 1490 D150 1573	OA E60 596 D150 594 OA E90 281 D150 302 RA E90 217 D150 255	OA E60 1133 D150 1208 OA E90 565 D150 532 RA E90 573 D150 567
072	At least 50 years RA with at least 4 of 7 ARA criteria	Female 80% White 64% Mean age 61 years Age range 40 to 92 years	52+ Compliance 97% E30 19.3 m/3275 py Dic 150 19.1 m/3262 py	E90 2032 Dic 150 2054	E90 1028 Dic 150 1045	E90 122 Dic 150 162	E90 419 Dic 150 397

Cause of discontinuations

Time to discontinuation

Laboratory AE	GI AE	Oedema AE	Hypertension AE	Serious AE	All cause	Lack of efficacy	Adverse event
E 0 Diclo 1	E 5 Diclo 3	E 2 Diclo 0	E2 Diclo 2	E 3 Diclo 0	wk E D 1 253 252 2 251 251 3 247 249 4 245 241 5 243 235 6 241 232	wk E D 1 256 259 2 256 259 3 256 255 4 255 253 5 255 253 6 255 253	
E 60 0 Diclo 150 0	E 60 6 Diclo 150 6	E 60 4 Diclo 150 1	E 60 0 Diclo 150 0	E 60 1 Diclo 150 0	wk E D 1 222 218 2 213 206 3 208 202 4 206 198	wk E D 1 222 222 2 222 215 3 222 215 4 222 215	wk E D 1 222 222 2 215 215 3 211 213 4 208 206
E 5 0 E10 1 E30 0 E60 0 E90 0 Pbo 0	E 5 0 E10 1 E30 1 E60 1 E90 3 Pbo 0	E 5 0 E10 0 E30 0 E60 0 E90 1 Pbo 0	E 5 0 E10 0 E30 0 E60 0 E90 0 Pbo 0	E 5 2 E10 3 E30 3 E60 4 E90 7 Pbo 2		wk E30 E60 P 1 102 111 59 2 101 111 57 3 99 111 54 4 98 110 53 5 98 110 53 6 98 110 53	wk E30 E60 P 1 102 112 60 2 102 110 59 3 102 110 59 4 101 110 59 5 101 109 58 6 99 110 58
E90 0 E120 0 Nap 1000 0 Pbo 0	E90 1 E120 0 Nap 1000 Pbo 0	E90 0 E120 0 Nap 1000 Pbo 0	E90 0 E120 0 Nap 1000 0 Pbo 0	E90 2 E120 0 Nap 1000 2 Pbo 0		wk E90 E120 N1000 P 1 103 91 99 88 2 103 91 96 84 3 98 86 88 63 4 97 85 86 57 5 96 84 80 50 6 96 83 79 49	wk E90 E120 N1000 P 1 103 92 99 93 2 102 92 99 93 3 102 92 99 93 4 102 92 99 93 5 101 92 98 93 6 101 92 98 93

E10 1	E10 0	E10 0	E10 0	E10 0	wk E60 E90 P	wk E60 E90 P
E60 0	E60 4	E60 1	E60 0	E60 1	1 126 134 122	1 125 133 123
E90 0	E90 0	E90 0	E90 0	E90 3	2 126 134 117	2 123 131 122
E120 0	E120 3	E120 0	E120 0	E120 2	3 126 134 117	3 122 131 122
Pbo 0	Pbo 0	Pbo 0	Pbo 0	Pbo 3	4 126 134 116	4 122 131 122
					5 126 131 113	5 121 131 121
					6 126 131 113	6 121 131 121
					8 123 131 112	8 120 131 119
E60 0	E60 1	E60 0	E60 1	E60 3	wk E60 N1000 P	wk E60 N1000 P
N1000 1	N1000 2	N1000 1	N1000 0	N1000 1	1 222 218 54	1 222 216 56
Pbo 0	Pbo 0	Pbo 1	Pbo 0	Pbo 1	2 222 216 53	2 220 216 56
					3 220 214 49	3 218 214 56
					4 218 214 45	4 218 211 56
					5 213 209 45	5 218 209 55
					6 213 209 45	6 215 207 55
					8 213 209 45	8 211 207 55
					12 209 209 45	12 206 201 53
E60 0	E60 2	E60 0	E60 0	E60 0	wk E60 N1000 P	wk E60 N1000 P
N1000 0	N1000 18	N1000 0	N1000 0	N1000 7	1 224 221 55	1 224 217 54
Pbo 0	Pbo 2	Pbo 0	Pbo 0	Pbo 0	2 224 219 54	2 222 214 54
					3 222 219 53	3 220 212 52
					4 222 219 53	4 220 210 52
					5 222 217 52	5 220 206 52
					6 222 217 51	6 220 203 51
					8 222 214 51	8 220 201 51
					12 220 212 50	12 219 194 49
E90 1	E90 3	E90 1	E90 1	E90 4	wk E90 N1000 P	wk E90 N1000 P
Nap1000 1	Nap1000 4	Nap1000 0	Nap1000 1	Nap1000 1	1 323 170 317	1 320 168 320
Pbo 1	Pbo 4	Pbo 0	Pbo 0	Pbo 2	2 320 165 304	2 317 168 317
					3 297 148 229	3 317 167 313
					4 291 145 213	4 317 165 313
					5 275 128 178	5 313 163 310
					6 271 122 168	6 313 163 307
					8 268 121 162	8 313 163 307
					12 252 107 142	12 310 160 307

E90 0	E90 2	E90 0	E90 0	E90 0
Nap1000 0	Nap1000 2	Nap1000 0	Nap1000 1	Nap1000 1
Pbo 4	Pbo 2	Pbo 0	Pbo 0	Pbo 0

wk E90 N1000 P
 1 349 181 353
 2 349 179 343
 3 339 176 318
 4 335 176 311
 5 321 172 289
 6 318 170 286
 8 314 167 282
 12 311 161 261

wk E90 N1000 P
 1 353 179 357
 2 349 177 353
 3 349 177 350
 4 349 177 350
 5 346 177 346
 6 346 177 346
 8 346 176 343
 12 342 176 343

E120 0	E120 10	E120 0	E120 0	E120 2
Nap1000 0	Nap1000 22	Nap1000 0	Nap1000 1	Nap1000 1
Pbo 1	Pbo 1	Pbo 0	Pbo 0	Pbo 6

wk E120 N1000 P
 1 251 242 247
 2 248 242 247
 3 246 242 245
 4 243 242 245
 5 243 242 245
 6 243 242 245
 8 238 239 245
 12 236 239 242

wk E120 N1000 P
 1 248 242 245
 2 243 239 245
 3 243 237 240
 4 243 237 240
 5 241 234 240
 6 238 232 232
 8 238 232 220
 12 236 229 220

E120 2	E120 10	E120 1	E120 2	E120 2
Ibu 2400 0	Ibu 2400 11	Ibu 2400 1	Ibu 2400 0	Ibu 2400 3
Pbo 0	Pbo 9	Pbo 0	Pbo 0	Pbo 2

wk E120 Ibu2400 P
 1 221 226 233
 2 221 226 231
 3 221 226 231
 4 221 226 231
 5 221 226 231
 6 221 224 228
 8 219 224 228
 12 219 221 226

wk E120 Ibu2400 P
 1 219 226 233
 2 219 224 231
 3 217 221 228
 4 212 221 228
 5 212 221 226
 6 208 219 226
 8 203 215 224
 12 201 210 221

E60 2	E60 4	E60 0	E60 0	E60 0
E90 3	E90 3	E90 1	E90 0	E90 1
Pbo 2	Pbo 1	Pbo 0	Pbo 0	Pbo 0

wk E60 E90 P
 1 105 104 107
 2 103 104 104
 3 102 104 101
 4 102 104 97
 5 99 102 97
 6 99 102 97
 8 98 101 93
 12 96 99 92

wk E60 E90 P
 1 105 104 108
 2 104 98 106
 3 102 96 105
 4 101 94 102
 5 98 93 102
 6 96 93 102
 8 96 92 101
 12 91 91 99

E60 2 E60 1 E60 2 E60 1 E60 1
E90 5 E90 4 E90 1 E90 2 E90 1
Pbo 1 Pbo 4 Pbo 1 Pbo 0 Pbo 1

wk E60 E90 P
1 103 106 107
2 100 105 99
3 100 100 97
4 100 99 96
5 99 99 92
6 99 98 91
8 98 96 86
12 97 95 81

wk E60 E90 P
1 101 107 107
2 97 104 107
3 94 101 107
4 93 100 107
5 93 96 106
6 92 95 106
8 92 93 105
12 89 89 96

E90 0 E90 7 E90 1 E90 2 E90 1
Cel 400 0 Cel 400 2 Cel 400 0 Cel 400 0 Cel 400 3
Ibu 2400 0 Ibu 2400 6 Ibu 2400 1 Ibu 2400 0 Ibu 2400 0
Pbo 0 Pbo 0 Pbo 0 Pbo 0 Pbo 0

wk E90 C400 I2400 P
6 105 105 103 101
12 103 104 103 98

wk E90 C400 I2400 P
6 102 98 98 103
12 96 96 96 102

E30 0 E30 3 E30 0 E30 2 E30 2
Ibu 2400 2 Ibu 2400 Ibu 2400 3 Ibu 2400 3 Ibu 2400 2
Pbo 0 11 Pbo 0 Pbo 1 Pbo 0
Pbo 2

wk E30 Ibu2400 P
1 212 208 102
2 210 206 95
3 208 197 86
4 203 191 81
5 199 187 75
6 197 187 74
8 195 185 73
12 188 176 71

wk E30 Ibu2400 P
1 214 206 103
2 212 204 102
3 210 200 102
4 210 197 102
5 208 195 101
6 208 195 99
8 208 189 97
12 201 183 96

E30 0 E30 4 E30 1 E30 2 E30 0
Ibu 2400 2 Ibu 2400 Ibu 2400 1 Ibu 2400 2 Ibu 2400 0
Pbo 2 10 Pbo 0 Pbo 0 Pbo 0
Pbo 8

wk E30 Ibu2400 P
1 222 213 219
2 222 211 206
3 220 207 197
4 215 204 192
5 211 200 181
6 211 200 179
8 208 198 177
12 204 194 177

wk E30 Ibu2400 P
1 220 211 221
2 217 207 217
3 217 198 208
4 217 196 208
5 217 194 206
6 217 194 206
8 215 194 206
12 213 192 206

E30 1 E30 3 E30 1 E30 2 E30 1
C200 2 C200 2 C200 1 C200 0 C200 2
Pbo 0 Pbo 0 Pbo 0 Pbo 0 Pbo 1

wk E30 C200 P
1 231 236 124
2 229 234 118
3 226 231 110
4 226 229 104
5 224 224 98
6 224 224 97
8 224 222 95
12 217 222 95

wk E30 C200 P
1 226 239 127
2 226 236 126
3 226 234 124
4 226 231 122
5 224 231 122
6 224 231 122
8 224 229 122
12 219 227 121

E30 0	E30 3	E30 1	E30 0	E30 0		wk E30 C200 P	wk E30 C200 P
C200 1	C200 2	C200 0	C200 0	C200 2		1 244 247 109	1 244 247 110
Pbo 0	Pbo 5	Pbo 0	Pbo 0	Pbo 3		2 242 245 101	2 244 247 109
						3 239 235 92	3 242 245 106
						4 237 232 83	4 242 245 106
						5 232 230 82	5 242 240 106
						6 229 230 80	6 242 240 106
						8 229 227 78	8 239 240 105
						12 229 225 76	12 239 240 103

E90 23	E90 262	E90 33	E90 81	E90 109	No data	data unextractable	no data
Dic 150 194	Dic 150 498	Dic 150 26	Dic 150 23	Dic 150 104			

OA	OA	OA	OA	OA	Overall	No data	Data on clinical plus laboratory only
E60 86	E60 213	E60 56	E60 146	E60 404	treatment group		
D150 175	D150 369	D150 49	D150 109	D150 400	all cause		
OA	OA	OA	OA	OA	discontinuation -		
E90 61	E90 134	E90 41	E90 55	E90 201	plus dease and		
D150 135	D150 195	D150 17	D150 24	D150 166	dose		
RA	RA	RA	RA	RA			
E90 48	E90 96	E90 28	E90 69	E90 243			
D150 81	D150 169	D150 16	D150 46	D150 196			

E90 23	E90 125	E90 23	E90 51	E90 129	No data	data unextractable	data unextractable
Dic 150 44	Dic 150 179	Dic 150 8	Dic 150 31	Dic 150 127			