**Appendix 4 Study and population characteristics**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Country** | **Interventions,n1****(route, total dosage/kg, duration)** | **Gestational age****(week)2** | **Birth weight(gram)2** | **Postnatal age at entry (day)2** | **Other medicines(n,%)** |
| **Dexamethasone vs Placebo** |
| **Kothadia 1999,**1**O'shea 1999,**2**O'shea 2007**3 | USA | Dexamethasone,57(iv,7.659mg/kg,42 days) | 26(23-29)3 | 740(456-1352) 3 | 19(15-27) 3 | Prenatal corticosteroids (20, 35)Surfactant (56, 99) |
| Placebo,61 | 25(23-31) 3 | 760(515-1324) 3 | 20(15-30) 3 | Prenatal corticosteroids (13, 21)Surfactant (61, 100) |
| **Yeh 1997,**4**Yeh 1998,**5**Yeh 2004,**6**Lin 2005**7 | Taiwan | Dexamethasone,132(iv, 6.16 mg/kg,28 days) | 29.5,2.7 | 1286,345 | NR4 | Prenatal corticosteroids(39, 29.5) |
| Placebo,130 | 29.2,2.6 | 1312,361 | NR | Prenatal corticosteroids(44, 33.8) |
| **Lin 1999**8 | Taiwan | Dexamethasone,20(iv,6.16 mg/kg,28 days) | 28.3, 3.0 | 1046, 294 | 7.8, 4.0 | Surfactant (20,100) |
| Placebo,20 | 28.4, 2.7 | 1087, 209 | 8.0, 4.6 | Surfactant (20,100) |
| **Wang 1996**9 | Taiwan | Dexamethasone,34(iv, 5.95mg/kg,21 days) | 28, 2.7 | 1392, 237 | NR  | NR |
| Placebo,29 | 29, 2.9 | 1378, 344 | NR  | NR |
| **Romagnoli 1999,** 10**Romagnoli 2002 a**11 | Italy | Dexamethasone,15(iv, 4.75 mg/kg, 14 days) | 27.5, 1.4 | 850, 183 | NR | Prenatal corticosteroids (6, 40) |
| Placebo,15 | 27.1, 1.4 | 948, 239 | NR | Prenatal corticosteroids (7, 46.6) |
| Dexamethasone,15(iv, 2.38 mg/kg, 7 days) | 27.7, 2.0 | 926, 230 | NR | Prenatal corticosteroids (9, 60) |
| Placebo,15 | 27.6, 1.5 | 931, 209 | NR | Prenatal corticosteroids(10, 66.6) |
| **Kari 1993,** 12**Mieskonen 2003**13 | Finland | Dexamethasone,17(iv,3.5mg/kg,7 days) | 27, 2 | 880, 194 | 14, 3 | Prenatal corticosteroids (1, 5.9)Surfactant (3, 17.6) |
| Placebo,21 | 27, 2 | 880, 194 | 13, 3 | Prenatal corticosteroids (1, 4.8)Surfactant (1, 4.8) |
| **Rastogi 1996**14 | USA | Dexamethasone,36(iv,3.3mg/kg,12 days) | 28.8, 2 | 1097, 234 | 7.2, 2.7 | Prenatal corticosteroids (2, 5.6)Surfactant (36, 100) |
| Placebo,34 | 28.2, 2 | 1022, 226 | 7.2, 3 | Prenatal corticosteroids (4, 11.8)Surfactant (34, 100) |
| **Morales 1998**15 | USA | Dexamethasone,13(iv,3.3mg/kg,12 days) | 26.8, 0.8 | 840, 78 | NR | Surfactant (13, 100) |
| Placebo,17 | 26.8, 1.3 | 838, 93 | NR | Surfactant (17, 100) |
| **Tapia 1998**16 | Chile | Dexamethasone,55(iv, 2.79 mg/kg,12 days) | 29. 1,2 | 1176, 244 | NR | Prenatal corticosteroids (18, 33)Surfactant (55,100) |
| Placebo,54 | 28.7, 1.8 | 1074, 230 | NR | Prenatal corticosteroids (18, 33)Surfactant (54,100) |
| **Soll 2001**17 | USA | Dexamethasone,273(iv,2.7mg/kg,12 days) | 25.8, 0.1 | 750.5, 7.7 | NR | Prenatal corticosteroids (197, 72)Surfactant (273, 100) |
| Placebo,269 | 25.7, 0.1 | 742.4, 8.5 | NR | Prenatal corticosteroids (205, 76)Surfactant (269, 100) |
| **Suske 1996**18 | Germany | Dexamethasone,14(iv, 2.5mg/kg,5 days) | 30.6, 2.7 | 1446, 422 | NR  | Prenatal corticosteroids (6, 43)Surfactant (14,100) |
| Placebo,12 | 29.3, 2.2 | 1219, 292 | NR  | Prenatal corticosteroids (5, 42)Surfactant (12,100) |
| **Romagnoli 1999,** 19**Romagnoli 2002 b**20 | Italy | Dexamethasone,25(iv,2.375mg/kg,7 days) | 28(25-31)5 | 940(590-1250) 5 | NR | Prenatal corticosteroids (13, 52)Surfactant (Yes) |
| Placebo,25 | 28(25-30)5 | 940(610-1250) 5 | NR | Prenatal corticosteroids (11, 44)Surfactant (Yes) |
| **Zecca 2001**21 | Italy | Dexamethasone,25(iv, 2.375 mg/kg,7 days) | 27.5,2 | 899, 250 | NR | Prenatal corticosteroids (9,45) Surfactant (Yes) |
| Placebo,25 | 27.9, 1.5 | 965, 235 | NR | Prenatal corticosteroids (8, 40)Surfactant (Yes) |
| **Durand 1995**22 | USA | Dexamethasone,23(iv,2.35mg/kg,7 days) | 27.4, 1.6 | 887, 213 | 9.7, 2.6 | Surfactant (19, 83) |
| Placebo,20 | 27.4, 1.7 | 834, 201 | 8.9, 1.8 | Surfactant (18, 90) |
| **Walther 2003**23 | USA | Dexamethasone,17(iv, 1.9mg/kg,14 days) | 28.5, 1.7 | 993, 203 | NR  | Prenatal corticosteroids (13,76)Surfactant (17,100) |
| Placebo,19 | 28.6, 1.9 | 1029, 225 | NR  | Prenatal corticosteroids (8,42)Surfactant (19,100) |
| **Brozanski 1995,**24**Gilmour 2005**25 | USA | Dexamethasone,39(iv,≥1.5mg/kg,≥3 days) | 25.6, 1.87 | 794, 168.61 | 7 | Prenatal corticosteroids (8, 20.5)Surfactant (35, 89.7) |
| Placebo,39 | 26, 1.87 | 814, 149.88 | 7 | Prenatal corticosteroids (9, 23.1)Surfactant (34, 87.2) |
| **Shinwell 1996,**26**Shinwell 2000**27 | Israel | Dexamethasone,132(iv,1.5mg/kg,3 days) | 29, 2.30 | 1185, 402.12 | NR | Prenatal corticosteroids (35, 26.5)Surfactant (132, 100) |
| Placebo,116 | 29, 2.15 | 1174, 366.19 | NR | Prenatal corticosteroids (30, 25.9)Surfactant (116, 100) |
| **Garland 1999**28 | USA | Dexamethasone,118(iv,1.175mg/kgor 1.35mg/kg,3 days) | 26, 0.2 | 835, 19 | NR  | Prenatal corticosteroids (22,18.6)Surfactant (118,100) |
| Placebo,123 | 26.1, 0.2 | 825, 19 | NR  | Prenatal corticosteroids (24,19.5)Surfactant (123,100) |
| **Anttila 2005**29 | Finland | Dexamethasone,53(iv, 1 mg/kg,2 days) | 26.3, 1.4 | 781, 124 | NR | Prenatal corticosteroids (45, 87)Surfactant (48, 91) |
| Placebo,56 | 27.0, 1.5 | 772, 140 | NR | Prenatal corticosteroids (46, 82)Surfactant (50, 91) |
| **Sinkin 2000**30 | USA | Dexamethasone,189(iv,1mg/kg,1 day) | 26.3, 1.37 | 890, 261.21 | NR | Prenatalcorticosteroids(116, 61.4)Surfactant (189, 100) |
| Placebo,195 | 26.1, 1.40 | 864, 237.39 | NR | Prenatalcorticosteroids(104, 53.3)Surfactant (195, 100) |
| **Doyle 2006,** 31**Doyle 2007**32 | Australia, Canada, New Zealand | Dexamethasone,35(iv,0.89mg/kg,10 days) | 24 (24-25)6 | 652 (590-730) 6 | 23 (20-34) 6 | Prenatal corticosteroids(31, 88.6)Surfactant (33, 94.3) |
| Placebo,35 | 25 (24-26) 6 | 700 (612-790) 6 | 22 (13-28) 6 | Prenatal corticosteroids(31, 88.6)Surfactant (34, 97.1) |
| **Stark 2001,** 33**Stark 2014**34 | USA | Dexamethasone,111(iv,0.89mg/kg,10 days) | 25.3, 1.7 | 734, 131 | 0.29, 0.12 | Prenatal corticosteroids (82, 74)Surfactant (106, 95) |
| Placebo,109 | 25.4, 1.6 | 736, 135 | 0.28, 0.12 | Prenatal corticosteroids (82, 75)Surfactant (105, 96) |
| **Lauterbach 2006**35 | Poland | Dexamethasone,33(iv, 0.75mg/kg, 3 days) | 28.5, 2.0 | 1072, 199 | NR  | Prenatal corticosteroids (22,67)Surfactant (Yes) |
| Placebo,27 | 28.8, 2.05 | 1137, 222 | NR  | Prenatal corticosteroids (20,74)Surfactant (Yes) |
| **Sanders 1994**36 | USA | Dexamethasone,19(iv, 0.2mg/kg,1 day) | 26.2, 0.44 | 831, 54.6 | NR  | Prenatal corticosteroids (6, 32)Surfactant (14,74) |
| Placebo,21 | 26.9, 0.46 | 839, 49.1 | NR  | Prenatal corticosteroids (9, 43)Surfactant (16, 76) |
| **Kopelman 1999**37 | USA | Dexamethasone,37(iv, 0.2mg/kg,1dose) | 25.6, 0.2 | 773, 39 | NR  | Surfactant (28, 85) |
| Placebo,33 | 25.8, 0.2 | 736, 24 | NR  | Surfactant (29, 78) |
| **Hydrocortisone vs Placebo** |
| **Baden 1972**38 | Canada | Hydrocortisone,22(iv,30mg/kg,1 day) | 32.5, 0.6 | 1730, 134 | 0.14, 0.025 | NR |
| Placebo,22 | 31.8, 0.6 | 1767, 121 | 0.18, 0.03 | NR |
| **Parikh 2013,**39**Parikh 2015**40 | USA | Hydrocortisone,31(iv,17mg/kg,7 days) | 25 (24-26)5 | 677,107 | 17 (14 -19) 5 | Surfactant (31, 100) |
| Placebo,33 | 25 (24-27) 5 | 655,142 | 16 (13 -20) 5 | Surfactant (32, 97) |
| **Watterberg 2004,** 41**Watterberg 2007**42 | USA | Hydrocortisone,180(iv, 13.5 mg/kg,15 days) | 25.2, 1.5 | 731, 126 | NR | Prenatal corticosteroids (138, 77)Surfactant (152, 84) |
| Placebo,180 | 25.3, 1.7 | 734, 126 | NR | Prenatal corticosteroids (146, 81)Surfactant (158, 88) |
| **Peltoniemi 2005,** 43**Peltoniemi 2009,** 44**Peltoniemi 2016**45 | Finland | Hydrocortisone,25(iv,11.5mg/kg,10 days) | 26.7,1.6 | 888,204 | NR  | Prenatal corticosteroids (23,92)Surfactant (24,96) |
| Placebo,26 | 26.5,2.8 | 903,220 | NR  | Prenatal corticosteroids (25,96)Surfactant (23,89) |
| **Bonsante 2007**46 | Italy | Hydrocortisone,25(iv, 10.5mg/kg,12days) | 26.2(25.2-27.4) 5 | 840(700-1000) 5 | NR | Prenatal corticosteroids(13,52) |
| Placebo,25 | 26.5( 25.0-28.1) 5 | 900(730-1010) 5 | NR | Prenatal corticosteroids(17,68) |
| **Watterberg 1999**47 | USA | Hydrocortisone,20(iv,10.5mg/kg,12 days) | 25.2, 1.3 | 732, 135 | NR | Prenatal corticosteroids (17, 85) |
| Placebo,20 | 25.4, 1.5 | 770, 135 | NR | Prenatal corticosteroids (17, 85) |
| **Baud 2016**48 | France | Hydrocortisone,255(iv,7.5mg/kg,10 days) | Median 26.4 | Median 860 | Median 0.67 | Prenatal corticosteroids (238, 93) |
| Placebo,266 | Median 26.5 | Median 840 | Median 0.64 | Prenatal corticosteroids 246, 92) |
| **Budesonide vs Placebo** |
| **Bassler 2015**49 | 9 countries | Budesonide,437(inh,19.16±11.96mg,33.9±15.9 days) | 26.1, 1.3 | 798, 193 | Median 0.28 | Prenatal corticosteroids (388, 88.8) |
| Placebo,419 | 26.1, 1.2 | 803, 189 | Median 0.28 | Prenatal corticosteroids (383, 91.4) |
| **Merz 1999**50 | Germany | Budesonide,12(inh,>16mg,10 days or until the infants were extubated) | 28.0 (27-32) 5 | 1108(820-1420) 5 | NR  | Prenatal corticosteroids (7, 58)Surfactant (10, 83) |
| Placebo,11 | 29.0 (27-31) 5 | 1120(880-1480) 5 | NR  | Prenatal corticosteroids (7, 64)Surfactant (9, 82) |
| **Jonsson 2000**51 | Sweden | Budesonide,15(inh,>2.25mg/kg,42 days) | 25 (23-27) 5 | 766(525-1122) 5 | NR  | Prenatal corticosteroids (12, 80)Surfactant (14, 93) |
| Placebo,15 | 26 (24-29) 5 | 813(630-1227) 5 | NR  | Prenatal corticosteroids (10, 67)Surfactant (15, 100) |
| **Beclomethasone vs Placebo** |
| **Denjean 1998**52 | France | Beclomethasone,44(iv,28mg,28 days) | 27.6, 1.5 | 1060, 248 | NR | Prenatal corticosteroids(11, 25.6)Surfactant (34, 79.1) |
| Placebo,43 | 27.8, 1.6 | 1082, 260 | NR | Prenatal corticosteroids(11, 25.6)Surfactant (34, 79.1) |
| **Jangaard 2002**53 | Canada | Beclomethasone,30(inh,4.8 mg/kg,24 days) | 27.2, 2 | 882, 204 | NR | Prenatal corticosteroids (15, 50)Surfactant (19, 63) |
| Placebo,30 | 27.9, 2 | 917, 178 | NR | Prenatal corticosteroids (16, 53)Surfactant (25, 83) |
| **Zimmerman 2000**54 | USA | Beclomethasone,23(inh,2.52 mg,24 days) | 26, 2 | 910, 198 | NR | Prenatal corticosteroids (14, 70)Surfactant (15, 75.0) |
| Placebo,24 | 26, 2 | 802, 225 | NR | Prenatal corticosteroids(15, 78.9)Surfactant (18, 94.7) |
| **Cole 1999**55 | England | Beclomethasone,123(inh,0.63mg/kg,28days) | 26,2 | 800,193 | 5.7,3.4 | Prenatal corticosteroids(77,62.6)Surfactant(95,77.23) |
| Placebo,130 | 26,2 | 802,189 | 5.4,2.9 | Prenatal corticosteroids(68,52.3)Surfactant(97,74.6) |
| **Fluticasone vs Placebo** |
| **Fok 1999**56 | NR  | Fluticasone,27(inh,7mg,14 days) | 27.9, 0.5 | 993, 71 | NR  | Prenatal corticosteroids(15, 55.6)Surfactant (27, 100) |
| Placebo,26 | 27.1, 0.5 | 981, 71 | NR  | Prenatal corticosteroids (13, 50)Surfactant (26, 100) |
| **Dexamethasone vs Beclomethasone** |
| **Rozycki 2003**57 | USA | Dexamethasone+Placebo,15(iv,7.659mg/kg,42 days) | 26 (24-27) 5 | 773, 511.23 | NR | Prenatal corticosteroids (2, 13.3)Surfactant (15, 100) |
| Beclomethasone+Placebo,16(inh,0.0168-0.02583mg/kg,42 days) | 26 (23-29) 5 | 710, 592 | NR | Prenatal corticosteroids (1, 6.3)Surfactant (16, 100) |
| Beclomethasone+Placebo,15(inh,0.007-0.01295mg/kg,42 days) | 26 (24-30) 5 | 796, 588.69 | NR | Prenatal corticosteroids (3, 20)Surfactant (15, 100) |
| Beclomethasone+Placebo,15(inh,0.00336-0.00518mg/kg,42 days) | 25 (24-31) 5 | 760, 480.25 | NR | Prenatal corticosteroids (2, 13.3)Surfactant (15, 100) |
| **Dexamethasone vs Budesonide** |
| **Dimitriou 1997**58 | UK | Dexamethasone,20(iv/po,2.8mg/kg,10 days) | 27 (24-31) 5 | 818(425-1460) 5 | 27 (8-118) 5 | Prenatal corticosteroids (11, 55)Surfactant (12, 60) |
| Budesonide,20(inh,1mg,10 days) | 27 (24-30) 5 | 849(584-1270) 5 | 26 (5-97) 5 | Prenatal corticosteroids (12, 60)Surfactant (14, 70) |
| **Halliday 2001,**59**Wilson 2006**60 | Northern Ireland | Early Dexamethasone,135(iv/po,2.7mg/kg,12 days) | 27.4, 1.9 | 1017, 290 | NR | Prenatal corticosteroids (82, 61)Surfactant (128, 95) |
| Late Dexamethasone,150(iv/po,2.7mg/kg,12 days) | 27.1, 1.9 | 1007, 283 | NR | Prenatal corticosteroids (82, 55)Surfactant (138, 92) |
| Early Budesonide,143(inh,0.96mg/kg,12 days) | 27.3, 1.8 | 1010, 284 | NR | Prenatal corticosteroids (88, 62)Surfactant (133, 93) |
| Late Budesonide,142(inh,0.96mg/kg,12 days) | 27.0, 2.0 | 994, 279 | NR | Prenatal corticosteroids (89, 63)Surfactant (132, 93) |
| **Dexamethasone vs Dexamethasone** |
| **Cummings 1989,**61**Gross 2005**62 | USA | Dexamethasone,13(iv,7.659mg/kg,42 days) | 26, 2 | 818, 145 | 15, 2 | NR  |
| Dexamethasone,12(iv,2.997mg/kg,18 days)  | 26, 2 | 810, 208 | 15, 2 | NR  |
| Placebo,11 | 26, 2 | 854, 197 | 15, 2 | NR |
| **Odd 2004**63 | New Zealand | Dexamethasone,17(iv, 7.659mg/kg, 42days) | 24 (23–27) 5 | 669, 113 | NR  | NR  |
| Dexamethasone,16(iv, >2.7 mg/kg, >9 days) | 24 (23–26) 5 | 720, 130 | NR  | NR  |
| **Bloomfield 1998,**64**Armstrong 2002**65 | UK | Dexamethasone,19(iv, ≥7.659 mg/kg,3days) | 25.5 (23-30) 5 | 775(605-1170) 5 | NR  | Prenatal corticosteroids (13,68) |
| Dexamethasone,21(iv, >1.5 mg/kg,42 days) | 25.5 (23-30) 5 | 790(560-1060) 5 | NR  | Prenatal corticosteroids (13,62) |
| **Papile 1998**66 | USA | Dexamethasone,182(iv/po,4.0mg/kg,14days) | 25.7, 1.9 | 808, 187 | NR | Prenatal corticosteroids (53, 29)Surfactant (165, 91) |
| Dexamethasone,189(iv/po,4.0mg/kg,14days) | 25.6, 1.6 | 801, 182 | NR | Prenatal corticosteroids (51, 27)Surfactant (169, 89) |

Note:

1.Number at random for trials with short-term outcomes or number at long-term follow up for trials with only long-term outcomes.

2.Mean,SD.

3.Median,(5-95th percentiles)

4.NR: not report

5.Median (range)

6.Median (IQR)

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