

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
<i>Alendronate vs. placebo</i>						
Black 1996 <sup>55</sup> (FIT 1)	<p><i>Any AE:</i> PBO, 819/1005 (81.5%) ALN10mg/d, 724/1022 (70.8%)</p> <p><i>Withdrawals due to AE:</i> PBO, 96/1005 (9.6%) ALN10mg/d, 78/1022 (7.6%)</p> <p><i>Hospitalisation:</i> PBO, 300/1005 (29.9%) ALN10mg/d, 250/1022 (24.5%)</p> <p><i>Death:</i> PBO, 21/1005 (2.1%) ALN10mg/d, 24/1022 (2.3%)</p>	<p><i>Any UGI:</i> PBO, 402/1005 (40%) ALN10mg/d, 422/1022 (41.3%)</p> <p><i>Dyspepsia:</i> PBO, 158/1005 (15.7%) ALN10mg/d, 155/1022 (15.2%)</p> <p><i>Abdominal pain:</i> PBO, 98/1005 (9.8%) ALN10mg/d, 121/1022 (11.8%)</p> <p><i>Nausea:</i> PBO, 97/1005 (9.7%) ALN10mg/d, 96/1022 (9.4%)</p> <p><i>Oesophagitis:</i> PBO, 4/1005(0.4%) ALN10mg/d, 7/1022 (0.7%)</p> <p><i>Oesophageal ulcer:</i> PBO, 2/1005 (0.2%) ALN10mg/d, 3/1022 (0.3%)</p> <p><i>Duodenal ulcer,</i> PBO, 6/1005 (0.6%) ALN10mg/d, 2/1022 (0.2%)</p> <p><i>Acid regurgitation:</i> PBO, 71/1005 (7.1%) ALN10mg/d, 71/1022 (6.9%)</p> <p><i>Gastritis:</i> PBO, 20/1005 (2%) ALN10mg/d, 24/1022 (2.3%)</p> <p><i>Gastric ulcer:</i> PBO, 16/1005 (1.6%) ALN10mg/d, 7/1022 (0.7%)</p> <p><i>Other oesophageal:</i> PBO, 11/1005 (1.2%) ALN10mg/d, 16/1022 (1.6%)</p>				

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		<i>Other gastric:</i> PBO, 2/1005 (0.2%) ALN10mg/d, 4/1022 (0.4%)				
Cummings 1998 <sup>64</sup> (FIT II)	<i>Death:</i> PBO, 40/2218 (1.8%) ALN10mg/d, 37/2214 (1.7%) <i>Hospitalisation:</i> PBO, 596/2218 (26.9%) ALN10mg/d, 644/2214 (29.1%) <i>Withdrawals due to AE:</i> PBO, 227/2218 ALN10mg/d, 221/2214	<i>Any UGI:</i> PBO, 1047/2218 (47.2) ALN10mg/d, 1052/2214 (47.5%) <i>Abdominal pain:</i> PBO, 325/2218(14.7%) ALN10mg/d, 322/2057 (14.5%) <i>Oesophagitis:</i> PBO, 10/2218 (0.5%) ALN10mg/d, 19/2214 (0.9%) <i>Oesophageal ulcer:</i> PBO, 4/2218 (0.2%) ALN10mg/d, 4/2214(0.2%) <i>Acid regurgitation:</i> PBO, 194/2218 (8.7%) ALN10mg/d, 204/2214 (9.2%) <i>Other oesophageal:</i> PBO, 41/2218 (1.8%) ALN10mg/d, 44/2214 (2%)				
Greenspan 2003 <sup>68</sup>	<i>Hospitalisations:</i> PBO, 26/93 (28%) ALN10mg/d, 34/93 (37%)	<i>Dysphagia:</i> PBO, 2/93 (2.0%) ALN10mg/d, 3/93 (3.0%) <i>Oesophagitis:</i> PBO, 21/93 (23%) ALN10mg/d, 26/93 (28%) <i>Indigestion,</i> PBO, 4/93 (4%) ALN10mg/d, 6/93 (6%) <i>Heartburn:</i> PBO, 15/93 (16%) ALN10mg/d, 17/93 (18%)				<i>Myocardial infarction:</i> PBO, 1/93 (1.0%) ALN10mg/d, 2/93 (2.0%) <i>High blood pressure:</i> PBO, 3/93 (3.0%) ALN10mg/d, 5/93 (5.0%) <i>Deep venous thrombosis:</i> PBO, 0/93 (0%) ALN10mg/d, 1/93 (1%) <i>Menstrual spotting:</i> PBO, 9/93 (10%) ALN10mg/d, 7/93 (8%) <i>Menstrual Cramps:</i>

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						PBO, 0/93 (0%) ALN10mg/d, 0/93 (0%) <i>Endometrial biopsy:</i> PBO, 1/93 (1%) ALN10mg/d, 2/93 (2%) <i>Peripheral oedema:</i> PBO, 12/93 (13%) ALN10mg/d, 9/93 (10%) <i>Weight gain:</i> PBO, 8/93 (9%) ALN10mg/d, 6/93 (6%) <i>Chest pain:</i> PBO, 13/93 (14%) ALN10mg/d, 16/93 (17%) <i>Endometrial biopsy:</i> PBO, 1/93 (1%) ALN10mg/d, 2/93 (2%) <i>Breast tenderness:</i> PBO, 16/93 (17%) ALN10mg/d, 22/93 (24%) <i>Falls:</i> PBO, 42/93 (45%) ALN10mg/d, 52/93 (56%)
Greenspan 2002 <sup>67</sup>	<i>Any AE:</i> PBO, 153/164 (35.0%) ALN10mg/d, 152/163 (33.0%)	<i>Any UGI:</i> PBO, 57/164 (35%) ALN10mg/d, 54/163 (33%) <i>Any serious UGI:</i> PBO, 3/164 (1.9%) ALN10mg/d, 1/163 (0.6%)				

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Liberman 1995 <sup>76</sup>	<i>Withdrawals due to AE:</i> PBO, 24/397 (6%) ALN10mg/d, 8/196 (4.1%)	<i>Discontinue due to UGI:</i> PBO, 8/397 (2.0%) ALN10mg/d, 2/196 (1.0%) <i>Abdominal pain:</i> PBO, 19/397 (4.8%) ALN10mg/d, 13/196 (6.6%) <i>Nausea:</i> PBO, 16/397 (4%) ALN10mg/d, 7/196 (3.6%) <i>Dyspepsia:</i> PBO, 14/397 (3.5%) ALN10mg/d, 7/196 (3.6%)				<i>Musculoskeletal pain:</i> PBO, 10/397 (2.5%) ALN10mg/d, 8/196 (4.1%) <i>Constipation:</i> PBO, 7/397 (1.8%) ALN10mg/d, 7/196 (3.1%) <i>Diarrohea:</i> PBO, 12/397 (3.1%) ALN10mg/d, 4/196 (1.8%)
Orwoll 2000 <sup>83</sup>	<i>Serious AE:</i> PBO, 22/95 (23%) ALN10mg/d, 27/146 (18%) <i>Withdrawals due to AE:</i> PBO, 10/95 (11.0%) ALN10mg/d, 4/146 (3.0%)	<i>Any UGI:</i> PBO, 21/95 (22%) ALN10mg/d, 37/146 (25%) <i>Abdominal pain:</i> PBO, 4/95 (4%) ALN10mg/d, 12/146 (8%) <i>Dyspepsia:</i> PBO, 1/95 (1%) ALN10mg/d, 9/146 (6%) <i>Acid regurgitation:</i> PBO, 5/95 (5%) ALN10mg/d, 7/146 (5%) <i>Oesophagitis:</i> PBO, 1/95 (1%) ALN10mg/d, 1/146 (1%)				<i>Nervous system:</i> PBO, 19/95 (20%) ALN10mg/d, 37/146 (25%) <i>Skin:</i> PBO, 21/95 (22%) ALN10mg/d, 33/146 (23%) <i>Urogenital:</i> PBO, 16/95 (17%) ALN10mg/d, 25/146 (17%) <i>Respiratory:</i> PBO, 47/95 (49%) ALN10mg/d, 66/146 (45%) <i>Musculoskeletal:</i> PBO, 50/95 (53%) ALN10mg/d, 68/146 (47%) <i>Cardiovascular:</i> PBO, 16/95 (17%) ALN10mg/d, 23/146 (16%)



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Pols 1999 <sup>84</sup> (FOSIT)	<p><i>Any AE:</i> PBO, 643/958 (67.1%) ALN10mg/d, 662/950 (69.7%)</p> <p><i>Serious AE:</i> PBO, 63/958 (6.5%) ALN10mg/d, 60/950 (6.3%)</p> <p><i>Withdrawals due to AE:</i> PBO, 61/958 (6.4%) ALN10mg/d, 53/950 (5.6%)</p>	<p><i>Any UGI:</i> PBO, 185/958 (19.3%) ALN10mg/d, 202/950 (21.3%)</p> <p><i>Dyspepsia:</i> PBO, 2/958 (0.2%) ALN10mg/d, 24/950 (2.5%)</p> <p><i>Abdominal pain:</i> PBO, 81/958 (8.5%) ALN10mg/d, 95/950 (10%)</p> <p><i>Nausea:</i> PBO, 37/958 (3.9%) ALN10mg/d, 44/950 (4.6%)</p> <p><i>Acid regurgitation:</i> PBO, 24/958, (2.5%) ALN10mg/d, 22/950, (2.3%)</p> <p><i>Gastritis:</i> PBO, 20/958 (2.1%) ALN10mg/d, 26/950 (2.8%)</p> <p><i>Gastric ulcer:</i> PBO, 1/958 (0.1%) ALN10mg/d, 4/950 (0.4%)</p> <p><i>Reflux oesophagitis:</i> PBO, 3/958 (0.3%) ALN10mg/d, 4/950 (0.4%)</p> <p><i>Oesophagitis:</i> PBO, 3/958 (0.3%) ALN10mg/d, 4/950 (0.4%)</p> <p><i>Duodenal ulcer:</i> PBO, 3/958 (0.3%) ALN10mg/d, 0/950 (0%)</p> <p><i>Oesophagalgia:</i> PBO, 0/958 (0%) ALN10mg/d, 2/950 (0.2%)</p> <p><i>Odynophagia:</i> PBO, 1/958 (0.1%) ALN10mg/d, 0/950 (0%)</p> <p><i>Oesophageal stricture:</i> PBO, 0/958 (0%) ALN10mg/d, 1/950 (0.1%)</p>				

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Saag 1998 <sup>91</sup>	<p><i>Any AE:</i> PBO, 126/159 (79%) ALN10mg/d, 662/950 (69.7%)</p> <p><i>Serious AE:</i> PBO, 34/159 (21%) ALN10mg/d, 60/950 (6.3%)</p> <p><i>Withdrawals due to AE:</i> PBO, 8/159 (5%) ALN10mg/d, 53/950 (5.6%)</p>	<p><i>Any UGI:</i> PBO, 26/159 (16%) ALN10mg/d, 40/157 (25%)</p> <p><i>Serious UGI:</i> PBO, 2/159 (1%) ALN10mg/d, 2/157 (1%)</p> <p><i>Oesophageal irritation:</i> PBO, 4/159 (3%) ALN10mg/d, 3/157 (2%)</p> <p><i>Abdominal pain:</i> PBO, 8/159 (5%) ALN10mg/d, 15/157 (10%)</p> <p><i>Peptic ulcer:</i> PBO, 2/159 (1%) ALN10mg/d, 2/157 (1%)</p>				<p><i>Musculoskeletal pain:</i> PBO, 25/159 (16%) ALN10mg/d, 25/157 (16%)</p>
Bone 2000 <sup>57</sup>	<p><i>Any AE:</i> PBO, 45/50 (90%) ALN10mg/d, 80/92 (87%)</p> <p><i>Serious AE:</i> PBO, 5/50 (10%) ALN10mg/d, 13/92 (14%)</p> <p><i>Withdrawals due to AE:</i> PBO, 5/50 (10%) ALN10mg/d, 6/92 (6%)</p>	<p><i>Any UGI:</i> PBO, 11/50 (22%) ALN10mg/d, 25/92 (27%)</p> <p><i>Dyspepsia:</i> PBO, 3/50 (6%) ALN10mg/d, 7/92 (8%)</p> <p><i>Abdominal pain:</i> PBO, 2/50 (4%) ALN10mg/d, 7/92 (8%)</p> <p><i>Peptic ulcer:</i> PBO, 0/50 (0%) ALN10mg/d, 0/92 (0%)</p> <p><i>Oesophagitis:</i> PBO, 2/50 (4%) ALN10mg/d, 5/92 (5%)</p>				

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<i>Ibandronate vs. placebo</i>						
McClung 2009 <sup>80</sup> USA.	<p><i>Any AE:</i> PBO, 64/83 (77.1%) IBN150mg/m, 60/77 (77.9%)</p> <p><i>Serious AE:</i> PBO, 1/83 (1.2%) IBN150mg/m, 3/77 (3.9%)</p> <p><i>Withdrawals due to AE:</i> PBO, 3/83 (3.6%) IBN150mg/m, 7/77 (9.1%)</p>	<p><i>Any UGI:</i> PBO, 20/83 (24.1%) IBN150mg/m, 24/77 (31.2%)</p> <p><i>Dyspepsia:</i> PBO, 4/83 (4.8%) IBN150mg/m, 4/77 (5.2%)</p> <p><i>Reflux oesophagitis:</i> PBO, 3/83 (3.6%) IBN150mg/m, 4/77 (5.2%)</p> <p><i>Nausea:</i> PBO, 3/83 (3.6%) IBN150mg/m, 5/77 (6.5%)</p>	<p><i>Flu-like symptoms</i> PBO, 0/83 (0%) IBN150mg/m, 4/83 (5.2%)</p>			<p><i>Arthralgia:</i> PBO, 8/83 (9.6%) IBN150mg/m, 12/77 (15.6%)</p> <p><i>Myalgia:</i> PBO, 2/83 (2.4%) IBN150mg/m, 5/77 (6.5%)</p>
Chesnut 2004 <sup>45</sup> (BONE)	<p><i>Any AE:</i> PBO, 867/975 (88.9%) IBN2.5mg/d, 879/977 (90%)</p> <p><i>Serious AE:</i> PBO, 211/975 (21.6%) IBN2.5mg/d, 234/977 (24%)</p> <p><i>Withdrawals due to AE:</i> PBO, 183/975 (18.9%) IBN2.5mg/d, 181/977 (18.5%)</p> <p><i>Deaths:</i> PBO, 10/975 (1%) IBN2.5mg/d, 11/977 (1.1%)</p>	<p><i>Duodenal ulcer:</i> PBO, 9/975 (0.9%) IBN2.5mg/d, 1/977 (0.1%)</p> <p><i>Dyspepsia:</i> PBO, 89/975 (9.1%) IBN2.5mg/d, 111/977 (11.4%)</p> <p><i>Belching:</i> PBO, 2/975 (0.2%) IBN2.5mg/d, 4/977 (0.4%)</p> <p><i>Gastritis:</i> PBO, 21/975 (2.2%) IBN2.5mg/d, 22/977 (2.3%)</p> <p><i>Gastroenteritis:</i> PBO, 54/975 (5.5%) IBN2.5mg/d, 54/977 (5.5%)</p> <p><i>GI pain:</i> PBO, 25/975 (2.6%) IBN2.5mg/d, 19/977 (1.9%)</p> <p><i>Nausea:</i> PBO, 61/975 (6.3%) IBN2.5mg/d, 41/977 (4.2%)</p> <p><i>Oesophageal ulcer:</i> PBO, 1/975 (0.1%) IBN2.5mg/d, 2/977 (0.2%)</p> <p><i>Oesophageal stenosis:</i> PBO, 1/975 (0.1%)</p>				

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		IBN2.5mg/d, 0/977 (0%) <i>Oesophagitis:</i> PBO, 10/975 (1%) IBN2.5mg/d, 15/977 (1.5%) <i>Stomach ulcer:</i> PBO, 6/975 (0.6%) IBN2.5mg/d, 3/977 (0.3%) <i>Vomiting:</i> PBO, 24/975 (2.5%) IBN2.5mg/d, 29/977 (3%)				
<b><i>Risedronate vs. placebo</i></b>						
McClung 2001 <sup>78</sup> (HIPS)	<i>Any AE:</i> PBO, 2805/3134 (89.5%) RIS5mg/d, 2786/3104 (89.8%) <i>Serious AE:</i> PBO, 973/3134 (31%) RIS5mg/d, 943/3104 (30.3%) <i>Withdrawals due to AE:</i> PBO, 564/3134 (18.0%) RIS5mg/d, 550/3104 (17.7%)	<i>Any UGI:</i> PBO, 684/3134 (21.8%) RIS5mg/d, 657/3104 (21.2%) <i>Moderate to severe:</i> PBO, 258/3134 (8.3%) RIS5mg/d, 279/3104 (9%) <i>Abdominal pain:</i> PBO, 288/3134 (9.2%) RIS5mg/d, 250/3104 (8.1%) <i>Dyspepsia:</i> PBO, 254/3134 (8.1%) RIS5mg/d, 255/3104 (8.2%) <i>Oesophagitis:</i> PBO, 59/3134 (1.9%) RIS5mg/d, 54/3104 (1.7%) <i>Oesophageal ulcer:</i> PBO, 14/3134 (0.4%) RIS5mg/d, 9/3104 (0.3%)				
Fogelman 2000 <sup>66</sup> (BMD-MN)	<i>Any AE:</i> PBO, 172/180 (95.6%) RIS5mg/d, 169/177 (95.5%) <i>Serious AE:</i> PBO, 27/180 (15%) RIS5mg/d, 26/177 (15%) <i>Withdrawals due to AE:</i>	<i>Any UGI:</i> PBO, 47/180 (26.0%) RIS5mg/d, 40/177 (23.0%) <i>Abdominal pain:</i> PBO, 22/180 (12%) RIS5mg/d, 23/177 (13%) <i>Dyspepsia:</i> PBO, 18/180 (10.0%) RIS5mg/d, 15/177 (8%)				

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	PBO, 14/180 (8.0%) RIS5mg/d, 19/177 (11.0%)	<i>Oesophagitis:</i> PBO, 4/180, (2%) RIS5mg/d, 3/177, (2%) <i>Gastritis:</i> PBO, 0/180 (0%) RIS5mg/d, 3/177 (2%) <i>Oesophageal ulcer:</i> PBO, 1/180 (1%) RIS5mg/d, 3/177 (2%) <i>Stomach ulcer:</i> PBO, 5/180 (3%) RIS5mg/d, 1/177 (1%)				
Harris 1999 <sup>70</sup> (VERT-NA)	<i>Any AE:</i> PBO, 774/815 (95.0%) RIS5mg/d, 785/813 (97.0%) <i>Serious AE:</i> PBO, 219/815 (27%) RIS5mg/d, 237/813 (29%) <i>Withdrawals due to AE:</i> PBO, 136/815 (17.0%) RIS5mg/d, 138/812 (17.0%)	<i>Any UGI:</i> PBO, 219/815 (27.0%) RIS5mg/d, 245/813 (30.0%) <i>Moderate-to-severe UGI:</i> PBO, 102/815 (13%) RIS5mg/d, 106/813 (13%) <i>Dyspepsia:</i> PBO, 92/815 (11.0%) RIS5mg/d, 105/813 (12.9%) <i>Abdominal pain:</i> PBO, 97/815 (12%) RIS5mg/d, 103/813 (13%) <i>Gastritis:</i> PBO, 23/815 (3%) RIS5mg/d, 31/813 (4%) <i>Oesophagitis:</i> PBO, 13/815, (2%) RIS5mg/d, 11/813, (1%) <i>Duodenitis</i> PBO, 2/815 (0.2%) RIS5mg/d, 9/813 (1%)				
Sorensen 2003 <sup>100</sup> (VERT-NA extension)	<i>Serious AE:</i> PBO, 39/130 (30%) RIS5mg/d, 33/135 (24.4%) <i>Withdrawals due to AE:</i> PBO, 16/130 (12.3%)	<i>Any UGI:</i> PBO, 18/130 (13.8%) RIS5mg/d, 17/135 (12.2%) <i>Dyspepsia:</i> PBO, 4/130 (3.1%) RIS5mg/d, 9/135 (6.7%)				

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	RIS5mg/d, 10/135 (7.4%)	<i>Abdominal pain:</i> PBO, 7/130 (5.4%) RIS5mg/d, 7/135 (5.2%) <i>Oesophagitis:</i> PBO, 1/130 (0.8%) RIS5mg/d, 2/135 (1.5%) <i>Oesophageal ulcer:</i> PBO, 1/130 (0.8%) RIS5mg/d, 1/135 (0.7%) <i>Gastritis:</i> PBO, 3/130 (2.3%) RIS5mg/d, 1/135 (0.7%) <i>Gastric ulcer:</i> PBO, 1/130 (0.8%) RIS5mg/d, 0/135 (0%)				
Hooper 2005 <sup>72</sup> (VERT-MN)	<i>Any AE:</i> PBO, 115/125 (92.0%) RIS5mg/d, 122/129 (95.0%) <i>Serious AE:</i> PBO, 22/125 (18%) RIS5mg/d, 12/129 (9%) <i>Withdrawals due to AE:</i> PBO, 8/125 (6.0%) RIS5mg/d, 7/129 (5.0%)	<i>Any UGI:</i> PBO, 20/125 (16.0%) RIS5mg/d, 25/129 (19.0%) <i>Dyspepsia:</i> PBO, 12/125 (9.6%) RIS5mg/d, 8/129 (6.2%) <i>Abdominal pain:</i> PBO, 6/125 (4.8%) RIS5mg/d, 9/129 (7%) <i>Oesophagitis:</i> PBO, 4/125 (3.2%) RIS5mg/d, 4/129 (3.1%) <i>GI disorder:</i> PBO, 2/125 (1.6%) RIS5mg/d, 4/129 (3.1%)				
		<i>Gastritis:</i> PBO, 3/125 (2.4%) RIS5mg/d, 2/129 (1.6%) <i>Oesophageal ulcer:</i> PBO, 2/125 (1.6%) RIS5mg/d, 1/129 (0.8%) <i>Stomach ulcer:</i> PBO, 1/125 (0.8%) RIS5mg/d, 0/129 (0%)				

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
		<i>Duodenal ulcer:</i> PBO, 0/125 (0%) RIS5mg/d, 1/129 (0.8%)				
Reginster 2000 <sup>85</sup> (VERT-MN)	<i>Any AE:</i> PBO, 370/407 (91.0%) RIS5mg/d, 374/407 (92.0%) <i>Serious AE:</i> PBO, 135/407 (33%) RIS5mg/d, 151/407 (37%) <i>Withdrawals due to AE:</i> PBO, 81/407 (20%) RIS5mg/d, 63/407 (15%)	<i>Any UGI:</i> PBO, 104/407 (26.0%) RIS5mg/d, 109/407 (27.0%) <i>Abdominal pain:</i> PBO, 32/407 (8%) RIS5mg/d, 50/407 (12%) <i>Dyspepsia:</i> PBO, 44/407 (11.0%) RIS5mg/d, 36/407 (9.0%) <i>Oesophagitis:</i> PBO, 11/407 (3%) RIS5mg/d, 10/407 (2%) <i>Gastritis:</i> PBO, 14/407(3%) RIS5mg/d, 9/407(2%) <i>Stomach ulcer:</i> PBO, 2/407 (0.5%) RIS5mg/d, 6/407 (1%) <i>Duodenitis:</i> PBO, 0/407 (0%) RIS5mg/d, 2/407 (0.5%) <i>Oesophageal ulcer:</i> PBO, 3/407 (1%) RIS5mg/d, 2/407 (0.5%) <i>Duodenal ulcer:</i> PBO, 1/407 (0.5%) RIS5mg/d, 2/407 (0.5%)				<i>Cancer:</i> PBO, 17/407 (4.2%) RIS5mg/d, 19/407 (4.7%) <i>Cardiovascular:</i> PBO, 38/407 (9.3%) RIS5mg/d, 38/407 (9.3%)
Boonen 2009 <sup>58</sup>	<i>Any AE:</i> PBO, 68/93 (73%) RIS35mg/w, 134/191 (70%) <i>Serious AE:</i> PBO, 15/93 (16%) RIS35mg/w, 29/191 (15%) <i>Withdrawals due to AE:</i>	<i>Any UGI:</i> PBO, 17/93 (18%) RIS35mg/w, 16/191 (8%) <i>Moderate to severe UGI:</i> PBO, 4/93 (4%) RIS35mg/w, 6/191 (3%) <i>Constipation:</i> PBO, 5/93 (5%) RIS35mg/w, 16/191 (8%)	<i>Influenza:</i> PBO, 5/93 (5%) RIS35mg/w, 11/191 (6%)			<i>Arthralgia:</i> PBO, 8/93 (9%) RIS35mg/w, 11/191 (6%) <i>Back pain:</i> PBO, 2/93 (2%) RIS35mg/w, 13/191 (7%) <i>Nasopharyngitis:</i> PBO, 5/93 (5%) RIS35mg/w, 11/191 (6%)

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
	PBO, 9/93 (9.7%) RIS35mg/w, 7/191 (3.7%) <i>Death:</i> PBO, 3/93 (3%) RIS35mg/w, 2/191 (1%)					<i>Headache:</i> PBO, 0/93 (0%) RIS35mg/w, 10/191 (5%)
<b>Zoledronate vs. placebo</b>						
Black 2007 <sup>56</sup> (HORIZON-PFT)	<i>Any AE:</i> PBO, 3616/3852 (93.9%) ZOL5mg/y, 3688/3862 (95.5%) <i>Serious AE:</i> PBO, 1158/3852 (30.1%) ZOL5mg/y, 1126/3862 (29.2%) <i>Withdrawals due to AE:</i> PBO, 70/3852 (1.8%) ZOL5mg/y, 80/3862 (2.1%) <i>Death:</i> PBO, 112/3852 (2.9%) ZOL5mg/y, 130/3862 (3.4%)		<i>Flu-like symptoms:</i> PBO, 61/3852 (1.6%) ZOL5mg/y, 301/3862 (7.8%)	<i>Osteonecrosis of the jaw:</i> Reports that no cases of osteonecrosis of the jaw were observed	<i>Atrial fibrillation:</i> PBO, 73/3852 (1.9%) ZOL5mg/y, 94/3862 (2.4%) <i>Serious:</i> PBO, 20/3852 (0.5%) ZOL5mg/y, 50/3862 (1.3%)	<i>Pyrexia:</i> PBO, 79/3852 (2.1%) ZOL5mg/y, 621/3862 (16.1%) <i>Headache:</i> PBO, 90/3852 (2.3%) ZOL5mg/y, 273/3862 (7.1%) <i>Arthralgia:</i> PBO, 76/3852 (2.0%) ZOL5mg/y, 245/3862 (6.3%) <i>Myalgia:</i> PBO, 66/3852 (1.7%) ZOL5mg/y, 365/3862 (9.5%) <i>Myocardial infarction:</i> PBO, 45/3852 (1.2%) ZOL5mg/y, 38/3862 (1.0%)
Reid <i>et al.</i> , 2010 <sup>102</sup> (HORIZON-PFT) Adverse events in first three days following administration		<i>Any UGI:</i> PBO, 80/3852 (2.1%) ZOL5mg/y, 300/3862 (7.8%) <i>Abdominal pain:</i> PBO, 17/3852 (0.4%) ZOL5mg/y, 40/3862 (1.0%) <i>Anorexia:</i>	<i>Flu-like symptoms:</i> PBO, 49/3852 (1.3%) ZOL5mg/y, 303/3862 (7.8%) <i>Fever:</i> PBO, 70/3852 (1.8%)			<i>Eye inflammation:</i> PBO, 2/3852 (0.1%) ZOL5mg/y, 14/3862 (0.4%) <i>Eye pain:</i> PBO, 0/3852 (0.0%) ZOL5mg/y, 9/3862 (0.2%) <i>Dizziness/vertigo:</i> PBO,



Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
		PBO, 7/3852 (0.2%) ZOL5mg/y, 45/3862 (1.2%) <i>Diarrhoea:</i> PBO, 23/3852 (0.6%) ZOL5mg/y, 55/3862 (1.4%) <i>Nausea:</i> PBO, 37/3852 (1.0%) ZOL5mg/y, 158/3862 (4.1%) <i>Vomiting:</i> PBO, 6/3852 (0.2%) ZOL5mg/y, 73/3862 (1.9%)	ZOL5mg/y, 663/3862 (17.2%) <i>Chills:</i> PBO, 23/3852 (0.6%) ZOL5mg/y, 171/3862 (4.4%) <i>Any – fever, chills,            hot flush:</i> PBO, 96/3852 (2.5%) ZOL5mg/y, 785/3862 (20.3%)			40/3852 (1.0%) ZOL5mg/y, 75/3862 (1.9%) <i>Oedema peripheral:</i> PBO, 4/3852 (0.1%) ZOL5mg/y, 18/3862 (0.5%) <i>Syncope:</i> PBO, 0/3852 (0.0%) ZOL5mg/y, 7/3862 (0.2%) <i>Pain:</i> PBO, 11/3852 (0.3%) ZOL5mg/y, 74/3862 (1.9%) <i>Thirst:</i> PBO, 0/3852 (0.0%) ZOL5mg/y, 11/3862 (0.3%) <i>Insomnia:</i> PBO, 1/3852 (0.0%) ZOL5mg/y, 8/3862 (0.2%) <i>Tremor:</i> PBO, 2/3852 (0.1%) ZOL5mg/y, 11/3862 (0.3%) <i>Any body pains:</i> PBO, 180/3852 (4.7%) ZOL5mg/y, 770/3862 (19.9%) <i>Joint swelling:</i> PBO, 0/3852 (0.0%) ZOL5mg/y, 14/3862 (0.4%) <i>Musculoskeletal pain:</i> PBO, 73/3852 (1.9%) ZOL5mg/y, 190/3862 (4.9%) <i>Musculoskeletal stiffness:</i> PBO, 5/3852 (0.1%) ZOL5mg/y, 37/3862

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
						(1.0%) <i>Diffuse musculoskeletal pain:</i> PBO, 114/3582 (3.0%) ZOL5mg/y, 606/3862 (15.7%) <i>Nasopharyngitis:</i> PBO, 5/3852 (0.1%) ZOL5mg/y, 17/3862 (0.4%) <i>Headache:</i> PBO, 59/3852 (1.5%) ZOL5mg/y, 225/3862 (5.8%) <i>Malaise:</i> PBO, 16/3852 (0.4%) ZOL5mg/y, 45/3862 (1.2%) <i>Fatigue:</i> PBO, 63/3852 (1.6%) ZOL5mg/y, 205/3862 (5.3%)
Lyles 2007 <sup>77</sup> (HORIZON-RFT)	<i>Any AE:</i> PBO, 852/1057 (80.6%) ZOL5mg/y, 867/1054 (82.3%) <i>Serious AE:</i> PBO, 436/1057 (41.2%) ZOL5mg/y, 404/1054 (38.3%) <i>Withdrawals due to AE:</i> PBO, 18/1057 (1.7%) ZOL5mg/y, 21/1054 (2.0%) <i>Death:</i> PBO, 141/1057 (13.3%) ZOL5mg/y, 101/1054 (9.6%)		<i>Flu-like symptoms:</i> PBO, 3/1057 (0.3%) ZOL5mg/y, 6/1054 (0.6%)	<i>Osteonecrosis of the jaw:</i> Reports that no cases of osteonecrosis of the jaw were observed	<i>Atrial fibrillation:</i> PBO, 38/1057 (3.6%) ZOL5mg/y, 46/1054 (4.4%) <i>Stroke:</i> PBO, 38/1057 (3.6%) ZOL5mg/y, 46/1054 (4.4%)	<i>Serum creatinine &gt;0.5 mg/dl:</i> PBO, 50/900 (5.6%) ZOL5mg/y, 55/886 (6.2%) <i>Creatinine clearance &lt;30 ml/min:</i> PBO, 65/891 (7.3%) ZOL5mg/y, 72/882 (8.2%) <i>Arthralgia:</i> PBO, 23/1057 (2.2%) ZOL5mg/y, 33/1054 (3.1%) <i>Myalgia:</i> PBO, 9/1057 (0.9%) ZOL5mg/y, 33/1054 (3.1%) <i>Pyrexia:</i> PBO, 9/1057 (0.9%)

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
						ZOL5mg/y, 73/1054 (6.9%) <i>Headache:</i> PBO, 9/1057 (0.9%) ZOL5mg/y, 16/1054 (1.5%) <i>Myocardial infarction:</i> PBO, 17/1057 (1.6%) ZOL5mg/y, 13/1054 (1.2%)
Boonen 2012 <sup>59</sup>	<i>Any AE:</i> PBO, 466/611 (76.3) ZOL5mg/y, 534/588 (90.8) <i>Serious AE:</i> PBO, 154/611 (25.2) ZOL5mg/y, 149/588 (25.3) <i>Death:</i> PBO, 18/611 (2.9) ZOL5mg/y, 15/588 (2.6)			<i>Osteonecrosis of the jaw:</i> Reports that no cases of osteonecrosis of the jaw were observed		<i>Pyrexia:</i> PBO, 23/611 (3.8%) ZOL5mg/y, 143/588 (24.3%) <i>Myalgia:</i> PBO, 25/611 (4.1%) ZOL5mg/y, 129/588 (21.9%) <i>Headache:</i> PBO, 27/611 (4.4%) ZOL5mg/y, 82/588 (13.9%) <i>Arthralgia:</i> PBO, 68/611 (11.1%) ZOL5mg/y, 123/588 (20.9%) <i>Back pain:</i> PBO, 74/611 (12.1%) ZOL5mg/y, 84/588 (14.3%) <i>Myocardial infarction:</i> PBO, 2/611 (0.3%) ZOL5mg/y, 9/588 (1.5%) <i>Cardiac failure:</i> PBO, 4/611 (0.7%) ZOL5mg/y, 1/588 (0.2%) <i>Hypertension:</i> PBO, 46/611 (7.5%) ZOL5mg/y, 50/588 (8.5%) <i>Cardiac disorder:</i>

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
						PBO, 30/611 (4.9%) ZOL5mg/y, 31/588 (5.3%) <i>Angina pectoris:</i> PBO, 7/611 (1.1%) ZOL5mg/y, 6/588 (1.0%)
McClung 2009 <sup>79</sup>	<i>Any AE:</i> PBO, 186/202 (92.1%) ZOL5mg/y, 173/181 (95.6%)	<i>Nausea:</i> PBO, 16/202 (7.9%) ZOL5mg/y, 21/181 (11.6%)		<i>Osteonecrosis of the jaw:</i> Reports that no cases of osteonecrosis of the jaw were observed		<i>Urinary tract infection:</i> PBO, 25/202 (12.4%) ZOL5mg/y, 16/181 (8.8%) <i>Upper Respiratory tract infection</i> PBO, 23/202 (11.4%) ZOL5mg/y, 19/181 (10.5%) <i>Pyrexia:</i> PBO, 9/202 (45%) ZOL5mg/y, 38/181 (21.0%) <i>Chills:</i> PBO, 6/202 (3.0%) ZOL5mg/y, 33/181 (18.2%) <i>Fatigue:</i> PBO, 8/202 (4.0%) ZOL5mg/y, 18/181 (9.9%) <i>Headache:</i> PBO, 23/202 (11.4%), ZOL5mg/y, 37/181 (20.4%) <i>Nasopharyngitis:</i> PBO, 23/202 (11.4%) ZOL5mg/y, 17/181 (9.4%) <i>Arthralgia:</i> PBO, 39/202 (19.3%) ZOL5mg/y, 34/181 (18.8%) <i>Pain:</i> PBO, 7/202 (3.5%) ZOL5mg/y, 27/181 (14.9%) <i>Myalgia:</i>

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
						PBO, 14/202 (6.9%) ZOL5mg/y, 41/181 (22.7%) <i>Back pain:</i> PBO, 24/202 (11.9%) ZOL5mg/y, 30/181 (16.6%) <i>Pain in extremity:</i> PBO, 20/202 (9.9%) ZOL5mg/y, 29/181 (16.0%)
<b>Head-to-head – Zoledronate vs. risedronate</b>						
Reid 2009 <sup>88</sup> (HORIZON)	ZOL5mg/y vs. RIS5mg/d – treatment subgroup: <i>Any AE:</i> 211/272 (78%) vs. 186/273 (68%) <i>Serious AE:</i> 50/272 (18%) vs. 54/237 (20%) <i>Withdrawals due to AE:</i> 3/272 (1%) vs. 3/273 (1%) <i>Death:</i> 3/272 (1%) vs. 3/273 (1%)  ZOL5mg/y vs. RIS5mg/d – prevention subgroup: <i>Any AE:</i> 111/144 (77%) vs. 93/144 (65%) <i>Serious AE:</i> 26/144 (18%) vs. 23/144 (16%) <i>Withdrawals due to AE:</i> 6/144 (4%) vs. 3/144 (2%)	ZOL5mg/y vs. RIS5mg/d – treatment subgroup: <i>Upper abdominal pain</i> 16/272 (6%) vs. 9/273 (3%) <i>Abdominal pain</i> 7/272 (3%) vs. 6/273 (2%) <i>Dyspepsia</i> 15/272 (6%) vs. 13/273 (5%) <i>Nausea</i> 30/272 (11%) vs. 21/273 (8%) <i>Vomiting</i> 17/272 (6%) vs. 7/273 (3%) <i>Gastritis</i> 2/272 (1%) vs. 4/273 (1%) <i>Gastro-oesophageal reflux</i> 3/272 (1%) vs. 1/273 (<1%)  ZOL5mg/y vs. RIS5mg/d – prevention subgroup: <i>Upper abdominal pain</i> 5/141 (3%) vs. 4/141 (3%) <i>Abdominal pain</i> 3/141 (2%) vs. 2/141 (1%) <i>Dyspepsia</i> 8/141 (6%) vs. 5/141 (3%) <i>Nausea</i> 10/141 (7%) vs. 14/141 (10%)	<i>Flu-like symptoms</i> Treatment subgroup: ZOL5mg/y 15 (6%) RIS5mg/d 3 (1%)  Prevention subgroup: ZOL5mg/y 10 (7%) RIS5mg/d 1 (1%)	<i>Bone pain:</i> Treatment subgroup: ZOL5mg/y 13 (5%) RIS5mg/d 5 (2%)  Prevention subgroup: ZOL5mg/y 0 (0%) RIS5mg/d 4 (3%)  <i>Osteonecrosis of the jaw:</i> Reports that no cases of osteonecrosis of the jaw were observed	<i>Atrial fibrillation:</i> Treatment subgroup: ZOL5mg/y 0 (0%) RIS5mg/d 0 (0%)  Prevention subgroup: ZOL5mg/y 3 (2%) RIS5mg/d 0 (0%)	ZOL treatment, RIS treatment, ZOL prevention, RIS prevention: Worsening rheumatoid arthritis 21 (8%) 17 (6%) 5 (3%) 4 (3%) Constipation 5 (2%) 7 (3%) 4 (3%) 3 (2%) Diarrhoea 12 (4%) 10 (4%) 3 (2%) 0 (0%) Rectal haemorrhage 1 (<1%) 0 (0%) 3 (2%) 0 (0%) Urinary tract infection 16 (6%) 13 (5%) 5 (3%) 4 (3%) Back pain 14 (5%) 17 (6%) 4 (3%) 9 (6%) Hypertension 14 (5%) 11 (4%) 4 (3%) 6 (4%) Asthenia 9 (3%) 6 (2%) 7 (5%) 9 (6%) Anaemia 8 (3%) 10 (4%) 2 (1%) 2 (1%) Vertigo 6 (2%) 3 (1%) 2 (1%) 2 (1%) Fatigue 8 (3%) 4 (1%) 5

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
	<p><i>Death:</i> 1/144 (&lt;1%) vs. 0/144 (0%)</p>	<p><i>Vomiting</i> 3/141 (2%) vs. 3/141 (2%) <i>Gastritis</i> 3/141 (2%) vs. 2/141 (1%) <i>Gastro-oesophageal reflux</i> 2/141 (1%) vs. 5/141 (3%)</p>				<p>(3%) 2 (1%) Oedema peripheral 7 (3%) 6 (2%) 5 (3%) 3 (2%) Weight increase 7 (3%) 8 (3%) 2 (1%) 5 (3%) Pain in limbs 8 (3%) 2 (1%) 5 (3%) 3 (2%) Musculoskeletal chest pain 7 (3%) 0 (0%) 1 (1%) 0 (0%) Dizziness 7 (3%) 2 (1%) 3 (2%) 2 (1%) Sciatica 7 (3%) 0 (0%) 3 (2%) 1 (1%) Insomnia 7 (3%) 3 (1%) 1 (1%) 3 (2%) Rash 3 (1%) 7 (3%) 0 (0%) 1 (1%) Allergic dermatitis 2 (1%) 6 (2%) 0 (0%) 2 (1%) Palpitations 1 (&lt;1%) 0 (0%) 3 (2%) 3 (2%) Chest pain 1 (&lt;1%) 0 (0%) 1 (1%) 3 (2%) Cataract 3 (1%) 4 (1%) 4 (3%) 3 (2%) Keratoconjunctivitis sicca 0 (0%) 0 3 (2%) 0 (0%) Bronchitis 2 (1%) 1 (&lt;1%) 3 (2%) 5 (3%) Contusion 5 (2%) 1 (&lt;1%) 3 (2%) 1 (1%) Fall 4 (1%) 4 (1%) 3 (2%) 0 (0%) Musculoskeletal stiff ness 1 (&lt;1%) 0 (0%) 4 (3%) 1 (1%) Joint swelling 1 (&lt;1%) 2 (1%) 3 (2%) 0 (0%) Musculoskeletal pain 5</p>

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
						(2%) 2 (1%) 1 (1%) 5 (3%) Anxiety 1 (<1%) 3 (1%) 3 (2%) 2 (1%) Depression 4 (1%) 5 (2%) 3 (2%) 2 (1%) Proteinuria 4 (1%) 0 (0%) 0 3 (2%) Paraesthesia 2 (1%) 1 (<1%) 4 (3%) 1 (1%)
<b>Head-to-head – Alendronate vs. Ibandronate</b>						
Miller 2008 <sup>81</sup> (MOTION)	<p><i>Any AE:</i> ALN70mg/w, 659/859 (75.4%) IBN150mg/m, 632/874 (73.6%)</p> <p><i>Serious AE:</i> ALN70mg/w, 39/859 (4.5%) IBN150mg/m, 55/874 (6.4%)</p> <p><i>Death:</i> ALN70mg/w, 2/859 (0.2%) IBN150mg/m, 4/874 (0.5%)</p>	<p><i>Dyspepsia:</i> ALN70mg/w, 48/859 (5.6%) IBN150mg/m, 60/874 (6.9%)</p>	<p><i>Influenza:</i> ALN70mg/w, 36/859 (4.2%) IBN150mg/m, 49/874 (5.6%)</p>			<p><i>Nasopharyngitis:</i> ALN70mg/w, 41/859 (4.8%) IBN150mg/m, 51/874 (5.8%)</p> <p><i>Arthralgia:</i> ALN70mg/w, 49/859 (5.7%) IBN150mg/m, 47/874 (5.5%)</p> <p><i>Back pain:</i> ALN70mg/w, 45/859 (5.2%) IBN150mg/m, 60/874 (6.9%)</p> <p><i>Hypertension:</i> ALN70mg/w, 51/859 (5.9%) IBN150mg/m, 68/874 (7.8%)</p>
<b>Head-to-head – Alendronate vs. Risedronate</b>						
Rosen 2005 <sup>90</sup> (FACT)	<p><i>Any AE:</i> ALN70mg/w, 394/515 (76.5%) RIS35mg/w, 399/527 (76.1%)</p> <p><i>Serious AE:</i></p>	<p><i>Upper GI:</i> ALN70mg/w, 116/515 (22.5%) RIS35mg/w, 106/527 (20.1%)</p> <p><i>Causing discontinuation:</i> ALN70mg/w, 13/515 (2.5%) RIS35mg/w, 16/527, (3.0%)</p>				

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
	ALN70mg/w, 45/515 (8.7%) RIS35mg/w, 41/527 (7.8%) <i>Withdrawals due to AE:</i> ALN70mg/w, 33/515 (6.4%) RIS35mg/w, 33/527 (6.2%)					
Bonnick 2006 <sup>104</sup> (FACT)	<i>Any AE:</i> ALN70mg/w, 358/411 (87.1%) RIS35mg/w, 358/414 (86.5%) <i>Serious AE:</i> ALN70mg/w, 51/411 (12.4%) RIS35mg/w, 56/414 (13.5%) <i>Withdrawals due to AE:</i> ALN70mg/w, 9/411 (2.2%) RIS35mg/w, 9/414 (2.2%)	<i>Upper GI:</i> ALN70mg/w, 128/411 (24.8%) RIS35mg/w, 122/414 (22.9%)				
Reid 2006 <sup>87</sup> (FACTS)	<i>Any AE:</i> ALN70mg/w, 306/468 (65.4%) RIS35mg/w, 314/468 (67.1%) <i>Serious AE:</i> ALN70mg/w, 24/468 (5.1%) RIS35mg/w, 47/468 (10.0%) <i>Withdrawals due to AE:</i> ALN70mg/w, 20/468 (4.3%) RIS35mg/w, 28/468	<i>Any UGI:</i> ALN70mg/w, 95/468 (20.3%) RIS35mg/w, 94/468 (20.1%); <i>Serious UGI:</i> ALN70mg/w, 2/468 (0.4%) RIS35mg/w, 4/468 (0.9%)				



Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
	(6%)					
Reid 2008 <sup>105</sup> (FACTS) (Extension to Reid 2006 <sup>87</sup> ) Seventy-two of the original 75 international sites Merck & Co., Inc.	<i>Any AE:</i> ALN70mg/w, 301/403 (74.7 %) RIS35mg/w, 299/395 (75.7%) <i>Serious AE:</i> ALN70mg/w, 42/403 (10.4%) RIS35mg/w, 44/395 (11.1%) <i>Withdrawals due to AE:</i> ALN70mg/w, 5/403 (1.2%) RIS35mg/w, 5/395 (1.3%)	<i>Any UGI:</i> ALN70mg/w, 91/403 (22.6%) RIS35mg/w, 73/395 (18.5%) <i>Serious UGI:</i> ALN70mg/w, 3/403 (0.7%) RIS35mg/w, 2/395 (0.5%) <i>Discontinued because of UGI AE:</i> ALN70mg/w, 1/403 (0.2%) RIS35mg/w, 2/395 (0.5%)				
<b>Head-to-head – Alendronate vs. Zoledronate</b>						
Hadji 2012 <sup>69</sup> (ROSE)	<i>Any AE:</i> ALN70mg/w, 145/194 (74.7%) ZOL5mg/y, 320/408 (78.4%) <i>Serious AE:</i> ALN70mg/w, 21/194 (10.8%) ZOL5mg/y, 43/408 (10.5%) <i>Withdrawals due to AE:</i> ALN70mg/w, 19/194 (9.8%) ZOL5mg/y, 2/408 (0.5%)	<i>Any UGI:</i> ALN70mg/w, 57/194 (29.4%) ZOL5mg/y, 75/408 (18.4%) <i>Upper abdominal pain:</i> ALN70mg/w, 13/194 (6.7%) ZOL5mg/y, 12/408 (2.9%) <i>Dyspepsia:</i> ALN70mg/w, 14/194 (7.2%) ZOL5mg/y, 3/408 (0.7%) <i>Nausea:</i> ALN70mg/w, 11/194 (5.7%) ZOL5mg/y, 23/408 (5.6%)	<i>Flu-like symptoms:</i> ALN70mg/w, 5/194 (32.4%) ZOL5mg/y, 132/408 (32.4%)	<i>Bone pain:</i> ALN70mg/w, 7/408 (3.6%) ZOL5mg/y, 23/194 (5.6%)  <i>Osteonecrosis of the jaw:</i> Reports that no cases of osteonecrosis of the jaw were observed		<i>Chills:</i> ALN70mg/w, 3/194 (1.5%) ZOL5mg/y, 13/408 (3.2%) <i>Fatigue:</i> ALN70mg/w, 4/194 (2.1%) ZOL5mg/y, 24/408 (5.9%) <i>Pyrexia:</i> ALN70mg/w, 2/194 (1%) ZOL5mg/y, 21/408 (5.1%) <i>Arthralgia:</i> ALN70mg/w, 21/408 (10.8%) ZOL5mg/y, 55/194 (13.5%) <i>Musculoskeletal and connective tissue:</i> ALN70mg/w, 64/194 (33.0%)

Author details (trial acronym), time point	Any AE, serious AE, withdrawals due to AE, death – n/N (%)	Upper GI AE – n/N (%)	Flu-like symptoms – n/N (%)	Hypocalcaemia, atypical femoral fracture, bone pain, jaw osteonecrosis, conjunctivitis– n/N (%)	Stroke, atrial fibrillation – n/N (%)	Other– n/N (%)
						ZOL5mg/y, 186/408 (45.6%) <i>Back pain:</i> ALN70mg/w, 20/408 (10.3%) ZOL5mg/y, 53/194 (13.0%) <i>Osteoarthritis:</i> ALN70mg/w, 9/408 (4.6%) ZOL5mg/y, 15/194 (3.7%) <i>Pain in extremity:</i> ALN70mg/w, 5/408 (2.6%) ZOL5mg/y, 30/194 (7.4%)