<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Groups</th>
<th>Primary Outcome Measure</th>
<th>Primary Positive Outcome Results (n, %)</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Bartalena et al 1983 | 12 pts po steroid "a"  
12 pts ORT+ po steroid | OI                      | po steroid group: 4/12 (33%)  
ORT+ po steroid group: 10/12 (83%) | Active TED  
24 of the total 48 patients were randomized  
Mean decrease in OI: 4.8 vs 3.2 in favor of ORT+ po steroid group (p=0.005) |
| Marcocci et al 1991 | 15 pts ORT "b"  
15 pts ORT+ po steroid | OI                      | ORT group: 5/15 (38%)  
ORT+ po steroid group: 9/15 (69%) | Active TED  
12/13 pts in ORT+ po steroid group had improvement in soft tissue changes. 6/13 pts in ORT group had improvement in soft tissue changes  
The 1 pt in ORT+ po steroid group had improvement in optic neuropathy. The 1 pt in the ORT group with optic neuropathy had no improvement in optic neuropathy |
Prummel et al. 1993

- 28 pts ORT
- 28 pts po steroid

ORT group: 13/28 (46%)
po steroid group: 14/28 (50%)

- Moderately severe TED
- 4% in each group considered treatment failures
- Steroid group improved quicker than ORT group.
- Side effects more common in steroid group
- ORT group had more improvement in ocular motility.
- Steroid group had more improvement in soft tissue.
- No significant improvement in proptosis in either group

Mourtis et al. 2000

- 30 pts ORT
- 30 pts sham

ORT group: 2 (12%)
Sham group: 4 (21%)

- Moderately severe TED
- Greatest improvement was in diplopia.
- No difference in proptosis or eyelid swelling

Kahaly et al 2000

- 18 pts group A
- 22 pts group B
- 22 pts group C

Response to therapy: significant amelioration of at least three objective signs

Group A: 12/18 (67%)
Group B: 13/22 (59%)
Group C: 12/22 (55%)

- Moderately severe TED
- Decrease in proptosis and ocular motility was noted only in group A.
- 11% group A, 18% group B and 23% group C required steroids after ORT.
- 0% group A, 9% group B and 9% group C required orbital decompression after ORT.
- 17% group A, 14% group B and 9% group C required strabismus surgery after ORT.
Marcocci et al 2001\textsuperscript{\textdagger}\textsuperscript{101}  
41 pts ORT+ po steroid  
41 pts ORT+ iv steroid  
Changes in at least two major criteria (variations in proptosis and lid width of 2 mm or greater, appearance, disappearance, or change in the degree of diplopia, changes in the CAS 2 points or more, and changes on one tenth or more in visual acuity) and change in one minor criterion (soft tissue changes, self-assessment evaluation)  
ORT+ po steroid group: 26/41 (63.4%)  
ORT+ iv steroid group: 36/41 (87.8%)  
Moderately severe TED  
Significant reduction in proptosis, lid retraction and diplopia in both groups.  
iv group had a greater % of pts with complete resolution of double vision (48.1% vs 36.4%).  
Final CAS score was lower in the iv group.  
Greater % of pts in the iv group had improvement in optic neuropathy (11/14 vs 3/9)

Gorman et al 2002\textsuperscript{27}  
42 pts: First ORT randomized to one orbit. Six months later fellow orbit treated with ORT.  
Volume of extraocular muscle and fat  
Ocular movement and diplopia  
Lid retraction  
See comment section  
Moderate TED  
At 6 months there was no difference in any of the clinical parameters measured between the ORT treated and sham treated orbits.

Gerling et al 2003\textsuperscript{106}  
41 pts 2.4 Gy ORT\textsuperscript{n}  
40 pts 16 Gy ORT  
Appearance of eye region  
Exophthalmos  
Range of vertical eye motility  
Eye muscle thickness  
Patient complaints.  
See comment section.  
Active TED  
At 6 months there was no statistical difference between the two groups in any of the 5 outcome criteria  
All outcome measures in both groups improved
<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Group 1</th>
<th>Patient Group 2</th>
<th>Major Criteria</th>
<th>Minor Criteria</th>
<th>Response to Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prummel et al 2004</td>
<td>44 pts ORT</td>
<td>44 pts sham</td>
<td>Major criteria (change of 8° or more in monoocular duction in the most affected direction of gaze (mostly elevation), a change of one or more grades in the diplopia score, and a change in pinhole visual acuity of &gt;1 lines on the Snellen chart) and minor criteria were a change of 2 mm or more in lid aperture, a change of 2 mm or more in proptosis, and a change of one or more grades in soft tissue involvement on the color slides. A response to treatment was defined as very good if improvement in at least two major criteria, good if improvement in one major criterion, fair if improvement in two minor criteria, no change if no changes or a change in only one minor criteria, and worse if deterioration in at least one major or two minor criteria.</td>
<td>ORT group: 23/44 (52%)</td>
<td>Sham group: 12/44 (27%)</td>
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<td>Ng et al 2005</td>
<td>8 pts ORT+ steroid</td>
<td>7 pts steroid</td>
<td>NOSPECS</td>
<td>ORT+ steroid group: 7/8 (87.5%)</td>
<td>Steroid group: 4/7 (57%)</td>
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<td>Quality of life was improved in both groups.</td>
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<td>No difference in progression of mild disease between ORT or sham (14% vs 16%, respectively)</td>
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<td>No significant change in vision between the 2 groups</td>
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* change in lid fissure width >2 mm, proptosis >2 mm, eye muscle area > 5mm², or absence of diplopia in primary position (normgaze)

**ABBREVIATIONS**

TED: thyroid eye disease  
ORT: orbital radiotherapy  
CAS: clinical activity score  
OI: Ophthalmology index  
pts: patients  
iv: intravenous  
po: oral
TREATMENT PROTOCOLS

a ORT: cobalt radiotherapy (10 daily doses of 200 Gy/day, total 2000 Gy/orbit);
   Steroids: 70-80 mg/day oral methylprednisolone for 3 weeks. Dose gradually tapered by 5 mg/week until daily dosage of 20 mg, then the dose was subsequently reduced by 2.5-5 mg every 2-3 weeks. Treatment discontinued after 5-6 months.

b ORT: Linear accelerator (10 daily doses of 2 Gy/day over 2 weeks)
   Steroids: 100 mg/day oral prednisone for 7 days followed by gradual weekly reduction until a daily dose of 25 mg reached, then dose reduced by 5 mg every 2 weeks till discontinuation.

c ORT: Linear accelerator (10 daily doses of 2 Gy/day over 2 weeks);
   Steroids: 60 mg/day po prednisone for 2 weeks, 40 mg/day 2 weeks, 30 mg/day 2 weeks, 20 mg/day 2 weeks, taper by 2.5 mg/week until zero.

d ORT: Linear accelerator (20 Gy in 10 fractions over 12 days)

e ORT: Linear accelerator
   Group A= 20 fractions of 1 Gy weekly over 20 weeks (protracted protocol; total or cumulative dose, 20 Gy)
   Group B= 10 fractions of 1 Gy daily, 5 days a week over 2 weeks (short arm regimen; total dose, 10 Gy)
   Group C= 10 fractions of 2 Gy daily over 2 weeks (short arm; total dose, 20 Gy)

f ORT: Linear accelerator (total of 20 Gy was delivered to each orbit in 10 fractions over 2 wks);
   Steroids: 100 mg/day po prednisone for 7 days followed by gradual weekly reduction until a dose of 25 mg was reached; the dose was then tapered by 5 mg every 2 wk or iv methylprednisolone 15 mg/kg body weight for four cycles and then 7.5 mg/kg body weight for four cycles; each cycle consisted of two infusions on alternate day at 2 wk intervals. The duration of treatment was 14 weeks.

g ORT: Linear accelerator (total of 20 Gy to each orbit in 10 fractions over 12 days).

h ORT: Linear accelerator (8 divided fractions of 0.3 Gy daily over 16 days (total of 2.4 Gy) or 8 divided fractions of 2.0 Gy daily over 16 days (total of 16 Gy))

i ORT: Linear accelerator (10 divided fractions of 2 Gy daily over 2 wks)

j ORT: Linear accelerator (total of 20 Gy to each orbit in 10 fractions over 2 weeks);
   Steroids: iv methylprednisolone 500 mg/day for 3 days followed by 0.7 mg/kg oral prednisolone daily for 4 weeks. From week 5, the dose was reduced by
5 mg per week until it reached 5 mg per day and was then further reduced to 2.5 mg daily for 1 more week and then stop