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SSAT ST STEPHEN'S AIDS TRUST

Chemoradiotherapy of anal cancer in HIV patients causes prolonged CD4 cell count suppression

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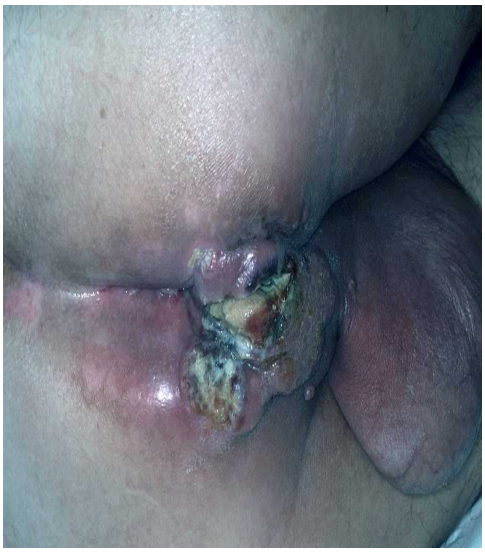
Background

- HIV is associated with a high risk of anal cancer
- Incidence does not correlate with a CD4 cell count
- Incidence is not declining despite highly active anti-retroviral therapy (HAART)



Method

- A prospective database 1986-2010 of 11,112 HIV+ patients (71,687 person-years of follow-up)
- 60 HIV+ patients with invasive anal cancer

Clinical features

	All	Pre-HAART	Post-HAART	P value
Number	60	8 (13%)	52 (87%)	
Male	59	8 (100%)	51 (98%)	0.16
Mean age (range)	44 years (28-75)	43 years (29-51)	45 years (28-75)	0.28
Prior AIDS defining illness	30 (50%)	3 (38%)	27 (52%)	0.43
Median CD4 cell count (range)	305 mm^{-3} (16-1252)	141 mm^{-3} (16-336)	332 mm^{-3} (46-1252)	0.02
On HAART at anal cancer diagnosis	41 (68%)	0 (0%)	41 (79%)	
On HAART with an undetectable viral load	32 (53%)	-	32 (78% of those on HAART)	

Features & Treatment

	All
Number	60
Performance status ECOG>2	11 (18%)
Histology:	
Squamous	53/60 (88%)
Basaloid	6/60 (10%)
Neuroendocrine	1/60 (2%)
Grade:	
Grade 1	8/44 (18%)
Grade 2	23/44 (52%)
Grade 3	13/44 (30%)
Not available	16/60 (27%)
Stage:	
1	23 (38%)
2	16 (27%)
3A	6 (10%)
3B	14 (23%)
4	1 (2%)
Treatment:	
Surgery alone (anal verge tumour)	6 (10%)
Radiotherapy alone	1 (2%)
Chemo-radiotherapy	50 (83%)
Best supportive care	3 (5%)

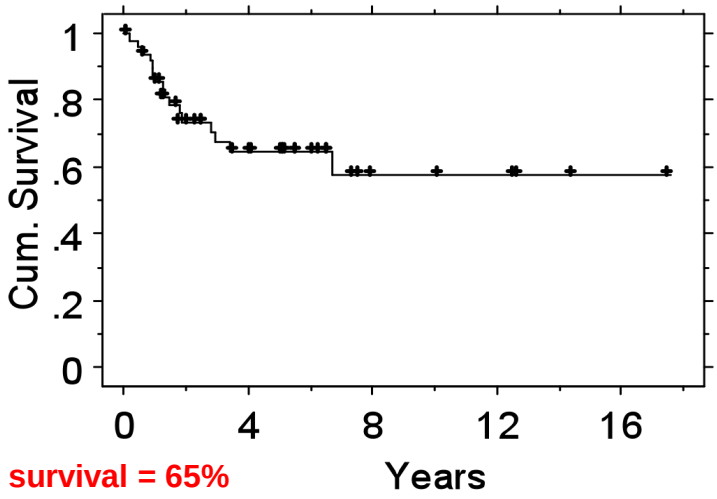
Chemoradiotherapy (CRT) & toxicity

- 50 patients, concurrent chemoradiotherapy (as in HIV –ve).
- 4 (8%) treatment interruptions for toxicity & 6 (12%) common toxicity criteria (CTC) grade 4 toxicities.
- No differences in toxicity grades between patients who were on a ritonavir boosted protease inhibitor regimen compared with other HAART therapies.
- No significant differences in toxicity grades between those with a CD4 cell count above and below 200mm^{-3} at anal cancer diagnosis.

Chemotherapy & response

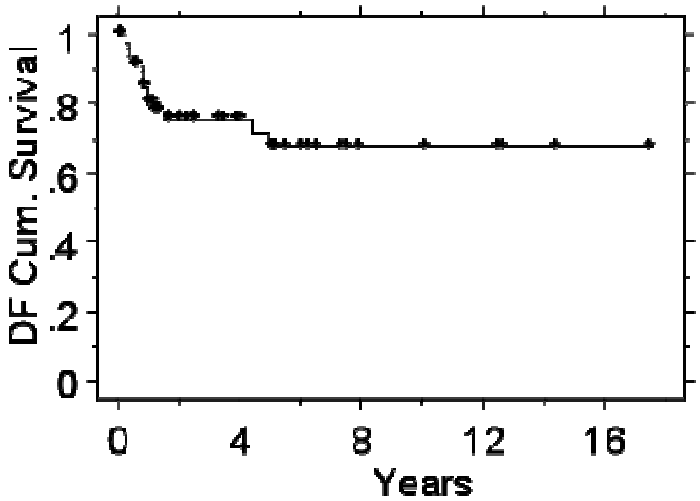
- Thirty three (67%) achieved a radiological complete response (CR), 13 (26%) a partial response (PR) and 4 (8%) patients had progressive disease.
- Ten patients relapsed, 3/33 achieving CR and 7/13 achieving PR ($p<0.0001$).

Overall Survival



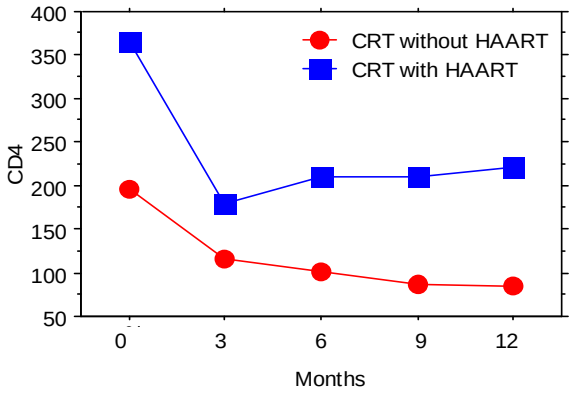
5 year overall survival = 65%
(95% Confidence Interval (CI) 51-78%)

Disease Free Survival



5 year disease free survival = 76%
(95% Confidence Interval (CI) 63-88%)

What does CRT do to CD4 counts?



Immunological Effects of CRT

- Median CD4 cell count fell by half during the first 3 months of therapy (P<0.0001) and remained below pre-CRT levels throughout a year of follow-up.
- These effects on CD4 cell count were irrespective of whether patients received concurrent HAART or not.
- No change in viral load for patients treated with CRT and HAART.

Mortality Data

- 19 (34%) patients died
- 13 from anal cancer
- 6 from HIV related illness while in remission
  - 2 Non-Hodgkins lymphoma
  - 1 Kaposi's sarcoma
  - 1 Progressive multifocal leucoencephalopathy & CMV infection
  - 1 Pneumocystis jiroveci pneumonia
  - 1 AIDS dementia complex & recurrent pneumonia

Conclusion

- This is the largest consecutive series in literature with a median follow-up of 6.5 years.
- Survival similar to recent smaller series reporting 5yr OS 61-67% but substantially better than older paper describing 5yr OS 20%.
- Survival similar to general population (UKCCCR ACT I study of 292 patients treated with CRT 5yr OS= 58%).

Conclusion

- CRT is associated with significant and prolonged suppression of CD4 despite HAART and suppressed viral load.

- This may cause late deaths in remission from opportunistic infections and AIDS defining malignancies.