A retrospective review of the benefits vs. safety implications of prednisolone during docetaxel chemotherapy alongside androgen deprivation therapy (ADT) in metastatic hormone-sensitive prostate cancer (mHSPC)

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Background

The benefit of adding docetaxel to lifelong ADT for mHSPC was established by three phase III trials; CHARRTED, STAMPEDED and GETUG-AFU 15. A key difference between these landmark trials was the addition of prophylactic prednisolone (5mg twice daily) in STAMPEDE but not CHAARTED or GETUG-AFU. This has led to mixed clinical practice. Potential toxicity from prolonged steroid use was recognised in a 2020 NHS England Safety alert. This study compared the toxicities in mHSPC patients treated in a tertiary centre with and without prednisolone alongside docetaxel and ADT.

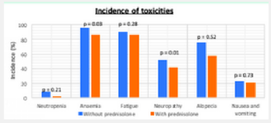
Methods

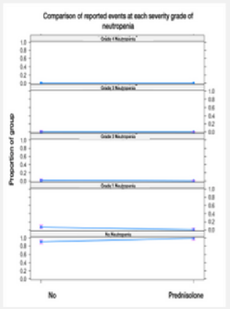
Electronic case notes of 299 mHSPC patients treated with docetaxel and ADT between February 2018 and September 2020 were reviewed 132 received prednisolone alongside docetaxel and ADT and 167 did not, as per clinician preference. Data on routinely collected blood counts and patient-reported, healthcare professional-graded (using CTCAE version 5 grading) toxicities. This data underwent statistical analysis using logistic regression, with robust standard errors, in RStudio.

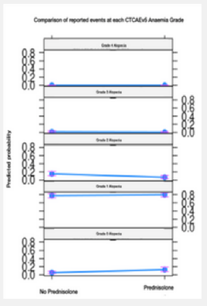
Toxicity	Incidence (% all grades)			Toxicity grades (%)				
	Without prednisolone	With prednisolone	P value	Without prednisolone		With prednisolone		P value
				G1/2	G3+	G1/2	G3+	
Neutropenia	8.5	0.1	0.21	6.7	0	0.1	0	0.01*
Neutropenic Sepsis	0	0.8	0.1					
Anaemia	95.9	85.6	0.03*	94.6	1.2	84.8	0.76	0.01*
Thrombocytopenia	1.8	0	0.2	1.8	0	0	0	0.98
Fatigue	90.4	86.3	0.28	87.4	3	84	2.3	0.47
Neuropathy	51.5	41.3	0.01*	47.2	4.3	40	1.3	0.06
Alopecia	75.9	57.1	0.52	75.3	0.6	57.1	0	<0.01*
Nausea and vomiting	22.3	20.4	0.73	22.3	0	18.2	0	0.72

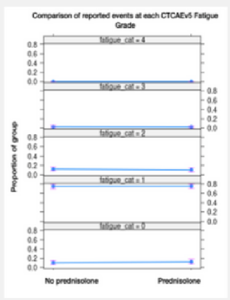
Results

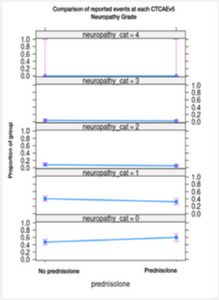
- 70.4% treated with prednisolone and 66.5% treated without prednisolone completed six cycles (p = 0.41).
- Incidence and severity of anaemia was greater in patients treated without prednisolone
- Incidence, but not severity, of neuropathy was greater in patients treated without prednisolone
- Severity, but not incidence, of alopecia was greater in patients treated without prednisolone
- Severity, but not incidence, of neutropenia was greater in patients treated without prednisolone
- There was no statistically signficiant difference in the incidence or severity fatigue or nausea and vomiting. There was no statiscally significant difference in the incidence of neutropenic sepsis.
- Patients treated with prednisolone had a statiscally signficant increase in contracts with healthcare services (P) through the Christie advice Hotline (P) or their General Practitioner (P). However, there was no difference found in the rates of hospital admissions between the two groups.
- Qualitative review of these healthcare interactions suggests many consultations were related to the administration of prednisolone.

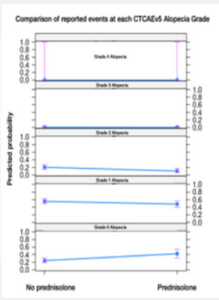


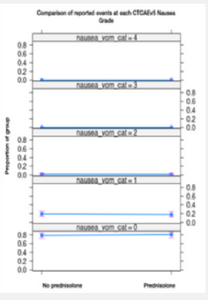












Conclusion

These findings suggest some clinical benefit in the addition of prednisolone to docetaxel and ADT in patients with mHSPC. However, prolonged prednisolone is associated with significant potential harms e.g. impaired blood glucose and adrenal insufficiency which may not justify these limited benefits.

These preliminary findings would benefit from further study with a larger sample size of patients treated at multiple centres. Outcome measure e.g. life expectancy was beyond the scope of this study and would benefit from further study.

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