Utilization and Safety of Concurrent Antibody-Drug Conjugates Alongside Extracranial Radiation Therapy in the Real-World Setting

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BACKGROUND

- Antibody-drug conjugates (ADCs) deliver targeted cytotoxic therapy but each agent has distinct toxicity driven by its linker, payload, and off-target effects.
- Concurrent ADC and radiation therapy (RT) use is increasing, yet safety data are limited.
- Early studies of trastuzumab deruxtecan (T-DXd), including TENDANCE, reported low acute toxicity with concurrent RT.
- Emerging evidence suggests higher dermatologic toxicity with trastuzumab emtansine (T-DM1) during concurrent RT, suggesting higher rates in KATHERINE, ATEMPT, and other prior cohorts.

Toxicity	Study	Sample size	% of positive symptoms
Skin erythema	Allali et al	8561	30.4%
Fatigue	Smet et al	993	35.8%
Peripheral neuropathy	Rades et al	133	27.8%

METHODS

1. Database extraction of nearly 200 patients that received concurrent RT and ADC within the past 10 years.
2. Excluded RT sites that didn't include breast, chest wall, and/or RNI.
3. Retrospective chart review of 87 patients to collect patient demographics, treatment characteristics, and toxicities.
4. Stratified analyses performed for each toxicity across age, menopause status, HR status, HER2 status, stage, ADC type, ADC timing, ECOG, RT type, and nodal RT.
5. Statistical testing used χ^2 or Fisher's exact tests, depending on cell counts.

OBJECTIVE

Evaluate the safety and tolerability of concurrent ADC and RT use in a real-world cohort to add and compare to the current, limited literature.

RESULTS

Table 1. Patient Characteristics (N = 87)

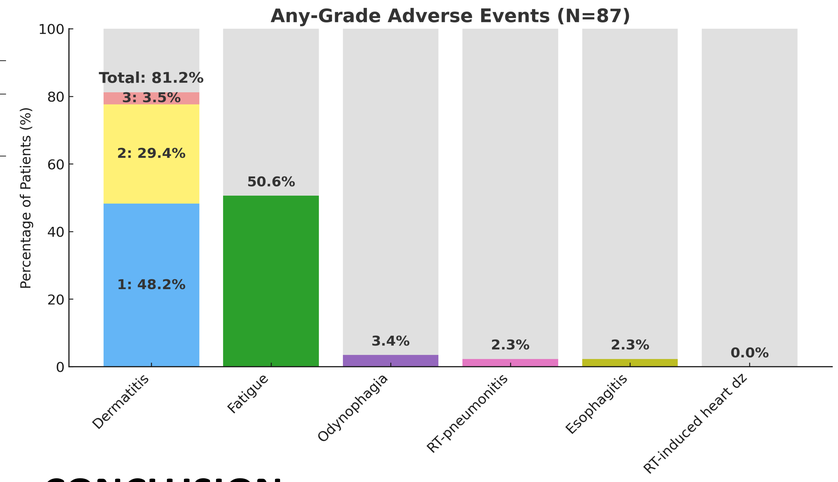
Characteristic	Value (% or range)
Age at RT, median	**53.0 (22–76)**
Follow-up, median	
• From ADC start	**8.97 mo (0–32.1)**
• From RT start	**1.18 mo (0.13–17.9)**
Stage	
• Stage 0	2 (2.3%)
• Stage 1	7 (8.0%)
• Stage 2	46 (52.9%)
• Stage 3	28 (32.2%)
• Stage 4	3 (3.4%)
• Unknown	1 (1.1%)
HR status	
• Positive	65 (74.7%)
• Negative	22 (25.3%)
HER2 IHC	
• Positive (3+)	52 (59.8%)
• Positive (2+)	22 (25.3%)
• Positive (no score)	3 (3.4%)
• Negative	10 (11.5%)

Table 2. Treatment Characteristics (N = 87)

Characteristic	Value (% or range)
ADC type	
• T-DM1	81 (93.1%)
• Trodelvy	4 (4.6%)
• T-DXd	2 (2.3%)
ADC timing	
• Before RT	6 (6.9%)
• During RT	81 (93.1%)
RT dose, median	**5000 cGy (1000–5600)**
Fractions, median	**25 (1–25)**
RT type / planning	
• 3D conformal/IGRT	59 (67.8%)
• IMRT/IGRT	18 (20.7%)
• 3D conformal	7 (8.0%)
• hexFRT	1 (1.1%)
• Enface electrons	1 (1.1%)
Nodal RT	
• Yes	65 (74.7%)
• No	22 (25.3%)

Table 3. Toxicities by Stratification

Toxicity	Stratification	Rates	p-value
Dermatitis	HER2 status (+ vs -)	84.2% vs 55.6%	0.060
Esophagitis	RT technique (IMRT/IGRT vs other)	11.1% vs 0%	0.097
Odynophagia	Age (≤52 vs >52)	7.0% vs 0%	0.116
Fatigue	Nodal RT (yes vs no)	54.9% vs 44.4%	0.337
Fatigue	Menopause status (pre vs post)	43.3% vs 55.8%	0.278



CONCLUSION

- Concurrent use of ADCs with breast and/or chest wall +/- RNI showed an increase incidence of dermatitis.
- Stratified analysis across age, menopause status, HR/HER2 status, stage, ADC type, ADC timing, ECOG, RT type, and nodal RT showed no statistically significant associations with acute toxicity.
- A trend toward increased dermatitis was observed in HER2+ patients (84.2% vs 55.6%, p = 0.060), and IMRT demonstrated a nonsignificant trend toward higher esophagitis (p = 0.097), but all findings were exploratory.

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