Tecentriq in Patients on Dialysis

This article responds to your request for information on the use of Tecentriq® (atezolizumab) in patients on dialysis. This response was developed according to the principles of evidence-based medicine and contains data from clinical literature.

In Brief

- The use of Tecentriq in patients on dialysis have not been formally established.
- The use of Tecentriq is not contraindicated in patients requiring dialysis.
- Atezolizumab has a large molecular weight (144.356 kDa) and should continue to circulate in serum after dialysis.
- Patients on dialysis were excluded from Roche pivotal clinical trials.
- Case reports of dialysis patients using Tecentriq are available.

Abbreviations

AE= Adverse event
eGFR= Estimated glomerular filtration rate
ES-SCLC= Extensive-stage small cell lung cancer
GU= Genitourinary
HD= Hemodialysis
IV= Intravenous
kDA= Kilodaltons
LCNEC= Large cell neuroendocrine carcinoma
NSCLC= Non-small cell lung cancer
PK= Pharmacokinetics
UC= Urothelial cell carcinoma

Considerations

The use of Tecentriq in patients requiring dialysis is not contraindicated, however the safety and efficacy has not been formally assessed. Administering Tecentriq to patients on dialysis would be a decision made by the treating physician, and should be based upon an appropriate risk-benefit assessment.

Tecentriq-related AEs with relevance to renal function were observed in Tecentriq clinical trials:[1]

- Blood creatinine increased (common, ≥ 1/100 to < 1/10)
- Nephritis (uncommon, ≥ 1/1000 to < 1/100)

Appropriate clinical caution and monitoring is recommended. Patients should be monitored for changes in renal function. Tecentriq should be used as described in the local label.

Pharmacokinetics

The pharmacokinetics of Tecentriq in patients on dialysis has not been formally established.

Roche's Phase 1 study assessing Tecentriq pharmacokinetics in patients with renal dysfunction did not include patients on dialysis.[1] Only 8 patients with severe renal impairment (eGFR 15 to 29 ml/min/1.73

m^2) were included, thus data on patients with severe renal impairment is too limited to formal conclusions in this patient population.

There were no clinically meaningful differences in the clearance of Tecentriq in patients with mild (eGFR 60 to 89 ml/min/1.73 m^2; n = 208) or moderate (eGFR 30 to 59 ml/min/1.73 m^2; n = 116) renal impairment compared with patients with normal renal function (eGFR greater than or equal to 90 ml/min/1.73 m^2; n = 140).

According to these results, no Tecentriq dose adjustments were recommended in patients with mild to moderate renal impairment.[1] See local label for further information on the PK of Tecentriq.

Permeability of dialysis membranes

Dialysis membranes are typically permeable to molecules up to 15 kDa. Larger molecules are retained by dialysis membranes.

As atezolizumab has a molecular weight of 144.356 kDa,[2] it should not be filtered out of the body during dialysis[3]. Tecentriq should therefore continue to circulate in serum after dialysis.

Clinical experience from Tecentriq pivotal trials

Patients on dialysis were excluded from Tecentriq pivotal clinical trials, including OAK[4], IMvigor210[5], and IMpower150[6], however patients with mild to moderate renal impairment were included.

The SAUL study was a single-arm, multicenter, international, open-label Phase 3b study that evaluated the safety and efficacy of Tecentriq 1,200 mg IV every three weeks in patients with previously treated, locally advanced or metastatic UC or non-urothelial carcinoma of the urinary tract.[7] The SAUL study included patients who were generally ineligible for clinical trials, such as those with renal impairment or requiring dialysis. 46 patients (5%) of patients in SAUL had severe renal dysfunction (creatinine clearance of <30 ml/min), however no patients requiring dialysis were enrolled.[8]

Case Reports

Table 1 provides information on published case reports of dialysis patients receiving Tecentriq.

Table 1: Case reports of patients receiving Tecentriq whilst on dialysis

Reference	Indication	Age	Therapy	Dialysis	Response	Grade 3/4 AEs
Parisi et al. 2019[9]	UC	Not reported	Tecentriq	HD	Partial response	None reported
Cheun et al. 2019[10]	UC	68	Tecentriq	HD	Progressive disease and septic shock	None reported
Hirsch et al. 2020[11]	UC	83	Tecentriq	HD	No progression	No immune related AEs reported
Mahmood et al. 2019[12]	NSCLC	74	Tecentriq	HD	Stable disease	None reported

Imaji et al. 2019[13]	ES-SCLC	80	Tecentriq and etoposide / carboplatin	HD	Significant shrinkage of tumour	Grade 4 neutropenia and leukopenia, chemotherapy was stopped
Stronbehn et al. 2020[14]	GU, Lung cancer	Not reported	Tecentriq	Not reported	Lung cancer patient had disease progression after 12 doses of Tecentriq q3w GU cancer patient had disease progression after 31 doses of Tecentriq q3w	None reported
Watari et al. 2021[15]	ES-SCLC	69, 73	Tecentriq and etoposide / carboplatin	HD	Both patients: Partial response	Patient 1: Grade 3 neutropenia, grade 3 thrombocytopenia, grade 3 anemia Patient 2: Febrile neutropenia
Cuenca et al. 2020[16]	UC	61	Tecentriq	Not reported	Over 12 months of treatment at time of publication	None reported
Kuo et al 2020[17]	UC	58	Tecentriq and Paclitaxel	HD	Progressive disease	None reported
	UC	45	Tecentriq and Paclitaxel	HD	Stable disease	None reported
	UC	66	Tecentriq	HD	Partial response	Grade 3 Tuberculosis Grade 4 Toxic epidermal necrolysis
Imai et al. 2023 [18]	LCNEC	70s	Tecentriq	HD	Partial response	None reported

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