Long-Term Survival with High Dose Interleukin-2 Therapy

SUPPLEMENTAL MATERIAL

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Table S1 - Guide to HD IL-2 Treatment Management

1. Patient Selection

- Physiologic patient selection is critical to safe administration and ability to tolerate the capillary leak syndrome produced by HD IL-2 administration
- Eligibility includes no or treated ischemic cardiac disease, reasonably normal pulmonary function and reasonably normal renal and hepatic function
- Patients with treated, asymptomatic brain metastases have safely received HD IL-2 (personal communication, investigators)
- Patients into their 70's have been successfully treated, having passed this physiologic screen

2. HD IL-2 Treatment Course (2 one week cycles separated by one week)

- T-cell growth factor (IL-2) activates T-cells, with many downstream effects
- Toxicity is predictable day by day of treatment cycle
- Common acute side effects are hypotension, capillary leak, malaise, diarrhea, oliguria, alterations in laboratory values which continue with continued treatment
- Acute toxicities subside/reverse when IL-2 dose is held, or treatment is stopped

3. HD IL-2 Treatment Centers

- Physicians and nurses experienced in management of cytokine-related toxicities
- Provision of monitored setting
- Some centers utilize:
  - Step down unit
  - Stem cell transplant unit – provides nursing intensity
  - Standard oncology unit, with monitoring capability
  - Will be same level of care as Car-T cell therapy

Table S2: Ongoing and Completed Trials of IL-2 and Anti-PD-1 Checkpoint Inhibitors

Metastatic Renal Cell Cancer		
NCT02964078	4 Blocks of 9 wks each: Pembro wk 1,4,7 HD IL-2, 5 doses over 33 hrs, wks 2,3, 5,6 starting second 9 wk block	Ref 24
NCT02989714	Wk 1, HD IL-2, cycle 1 Wk 2, Nivo Wk 3, HD IL-2, cycle 2 Wk 4 and every 2 wks, Nivo	
NCT03260504	Pembro, wk 1 and every 3 weeks; IL-2 – Cohort 1, SQ low dose wks 1-6; IL-2 – Cohort 2, low dose IV, wks 1 and 4 IL-2 – Cohort 3, HD IL-2, IV wks 1 and 4	
Metastatic Melanoma		
NCT02748564	Pembro, wk 0 and every 3 wks; IL-2 – Cohort 1, LD IV, wk 3 and 5 IL-2 – Cohort 2, Int Dose IV, wk 3 and 5 IL-2 - Cohort 3, HD IL-2 IV, wk 3 and 5	
NCT04165967	Adoptive TIL + Nivo + IL-2 in advanced melanoma	Swiss CT.Gov listing also
Metastatic Melanoma and Metastatic Renal Cell		
NCT03991130	Nivo day 1 and 35 Day 8-12 HD IL-2 cycle 1 Day 22-26 HD IL-2 cycle 2	

Anti-PD-1 – anti-programmed death-1; wk – week; Pembro - Pembrolizumab; HD IL-2 – high dose interleukin-2; Nivo – nivolumab; D – day; LD – low dose; SQ – subcutaneous; IV – intravenous; Int – intermediate; TIL – tumor infiltrating lymphocytes

TABLE S3 – PATIENT DEMOGRAPHICS

Characteristics	Metastatic Melanoma (n=54)	Metastatic Renal Cell (n=46)
Sex: Male/Female	31/23	36/10
Age: Median/range	53 years (25-76)	54 years (39-73)
Sites of Metastases:		
Lymph nodes	40%	20%
Lung	25%	50%
Liver	17%	4%
Bone	15%	11%
Other – CNS, pancreas, adrenal, spleen, soft tissue, GI tract	10% or less	10% or less

CNS – central nervous system, GI - gastrointestinal

TABLE S4 - TREATMENT RECEIVED
ONE COURSE = TWO 1-WEEK CYCLES

Courses (range 0.5-4 courses)	# Patients (n=100)
0.5 course	2
1 course	19
1.5 courses	5
2 courses	35
2.5 courses	6
3 courses	25
>3 courses	1
Unknown	7
2-3 courses	66