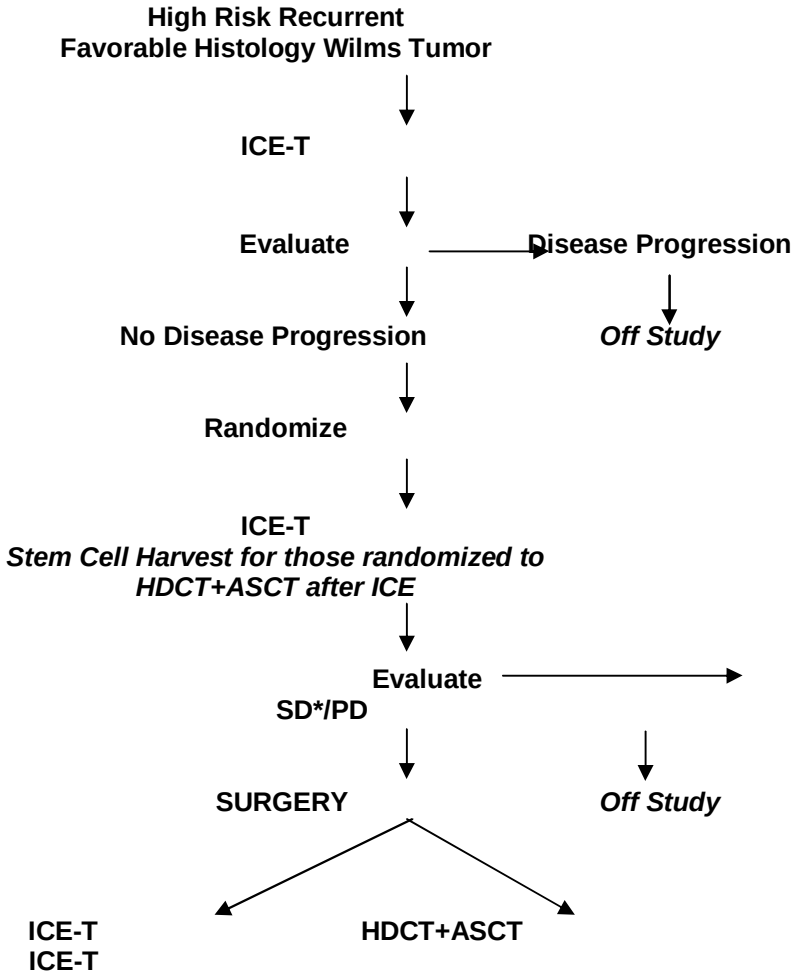
Arms / Regimens (include schema):

Schema



* SD w/o Differentiation or necrosis

Arms / Regimens

High-Risk WT

Induction:

Week 1	Week 4	Week 5	Week 7	Week 8	Week 10	Week 11	Week 12	Week 1
I	T	T	**Evaluation**	I	Stem cell harvest (if so randomized)	T	T	**Evalu and Su**
C				C				
E				E				

Drug	Rte	Dose		Day(s)
Ifosfamide (I)	IV over 1 hour	66.7 mg/kg/day for infants < 12 mo 2,000 mg/m² for children ≥ 12 mo		1-3
Carboplatin (CARBO)	IV over 1 hour	**GFR**	**Dose**	1
		> 150 mL/min/1.73m^2	560 mg/m^2 (18.7 mg/kg for infants)	
		100-150 mL/min/1.73m^2	500 mg/m^2 (16.6 mg/kg for infants)	
		75-99 mL/min/1.73m^2	370 mg/m^2 (12.3 mg/kg for infants)	
		50-74 mL/min/1.73m^2	290 mg/m^2 (9.7 mg/kg for infants)	
		30-49 mL/min/1.73m^2	200 mg/m^2 (6.7 mg/kg for infants)	
		<30 mL/min/1.73m^2	Hold carboplatin	
Etoposide (ETOP)	IV over 1 hour	3.3 mg/kg/day for infants < 12 mo. 100 mg/m^2/day for children ≥ 12 mo.		1-3
Topotecan (T)	IV over 30 minutes	1.8 mg/m²/day x 5 days x 2 weeks. Topotecan may be administered on an outpatient basis. It is expected that patients will become neutropenic (and sometimes febrile) before the 10th dose of topotecan. If the patient is clinically well, the topotecan may be continued to complete the planned 10 doses. **During the weeks of topotecan administration, stop trimethoprim/ sulfamethoxazole (TMP/SMX) one day prior to beginning the topotecan infusion.**		1-5 and 8-12
GCSF (following ICE): 5 mcg/kg/day subcutaneously from Day 4 through ANC >5,000/µL x 1 after 7 or more days of GCSF				
GCSF (following Topotecan): 5 mcg/kg/day subcutaneously from Day 14 through ANC >5,000/µL x 1 after 7 or more days of GCSF				
MESNA 400 mg/m²/dose IV as a loading dose with ifosfamide over 1 hour; then 400 mg/m²/dose as a 3 hour infusion followed by 400 mg/m²/dose boluses every 3 hours x 3 doses IV over 15-30 minutes on Days 1 through 3. (this would be 100% of Ifosfamide dose in our heavily pretreated patients)				
*Hydration: Prehydrate with D5 ½ NS at 125 mL/m^2/hr for 2 hr. Then continue at 125 mL/m^2/hr for 2 hr following completion of chemotherapy.				

Intensive Conventional Chemotherapy:

Week 15	Week 18	Week 19	Week 21	Week 24	Week 25	Week 27
I	T	T	I	T	T	**Evaluation and XRT**
C			C			
E			E			

Drug	**Rte**	**Dose**		**Day(s)**
Ifosfamide (I)	IV over 1 hour	66.7 mg/kg/day for infants < 12 mo 2,000 mg/m² for children ≥ 12 mo		1-3
Carboplatin (CARBO)	IV over 1 hour	**GFR**	**Dose**	1
		> 150 mL/min/1.73m^2	560 mg/m^2 (18.7 mg/kg for infants)	
		100-150 mL/min/1.73m^2	500 mg/m^2 (16.6 mg/kg for infants)	
		75-99 mL/min/1.73m^2	370 mg/m^2 (12.3 mg/kg for infants)	
		50-74 mL/min/1.73m^2	290 mg/m^2 (9.7 mg/kg for infants)	
		30-49 mL/min/1.73m^2	200 mg/m^2 (6.7 mg/kg for infants)	
		<30 mL/min/1.73m^2	Hold carboplatin	
Etoposide (ETOP)	IV over 1 hour	3.3 mg/kg/day for infants < 12 mo. 100 mg/m^2/day for children ≥ 12 mo.		1-3
Topotecan (T)	IV over 30 minutes	1.8 mg/m²/day x 5 days x 2 weeks. Topotecan may be administered on an outpatient basis. It is expected that patients will become neutropenic (and sometimes febrile) before the 10th dose of topotecan. If the patient is clinically well, the topotecan may be continued to complete the planned 10 doses. **During the weeks of topotecan administration, stop trimethoprim/ sulfamethoxazole (TMP/SMX) one day prior to beginning the topotecan infusion.**		1-5 and 8-12
GCSF (following ICE): 5 mcg/kg/day subcutaneously from Day 4 through ANC >5,000/µL x 1 after 7 or more days of GCSF				
GCSF (following Topotecan): 5 mcg/kg/day subcutaneously from Day 14 through ANC >5,000/µL x 1 after 7 or more days of GCSF				
MESNA 400 mg/m²/dose IV as a loading dose with ifosfamide over 1 hour; then 400 mg/m²/dose as a 3 hour infusion followed by 400 mg/m²/dose boluses every 3 hours x 3 doses IV over 15-30 minutes on Days 1 through 3. (this would be 100% of Ifosfamide dose in our heavily pretreated patients)				
*Hydration: Pre-hydrate with D5 ½ NS at 125 mL/m^2/hr for 2 hr. Then continue at 125 mL/m^2/hr for 2 hr following completion of chemotherapy.				

High-Dose Chemotherapy followed by Autologous Stem Cell Transplant:

Day	
-2	Melphalan
-1	
0	Transplant**

Drug doses during consolidation:

Melphalan	210 mg/ m² total dose over 1 hour

** DAY 0: 48 hours following chemotherapy completion - infusion procedure will be by institutional standard.

Hydration

Pre-hydrate with D5 ½ NS at 125 mL/m^2/hr for 3 hrs. Then continue at 125 mL/m^2/hr for 24 hr following completion of melphalan infusion. **GCSF infusion** (5 mcg/kg/day over 2 hours) begins four hours after stem cell infusion and continues daily until ANC is greater for 2,000/µL for 3 consecutive days.

Eligibility Criteria for Transplant

Patients must have sufficient stem cells available (defined as $\geq$ 3 x 10^6 CD34 cells/kg of PBSC or $\geq$ 1.5 x 10^8cells/kg mononuclear bone marrow cells). Hematopoietic progenitor cells-apheresis will be collected at Week 10 after ICE chemotherapy or as soon as feasible for patients randomized to receive HDT/ASCT. Patient will be receiving GCSF at 10 mcg/kg/day starting 24 hours following the completion of chemotherapy. Apheresis will be performed according to each institutional standard guideline. If the targeted $CD34^+$ cells cannot be obtained after a maximum of three collections, then apheresis will be repeated following the second cycle of ICE chemotherapy. If the targeted $CD34^+$ cells are not achieved, then autologous bone marrow harvest should be performed.

- Total bilirubin $\leq$1.5 x normal, and SGOT (AST) or SGPT (ALT) <2.5 x normal.
- GFR > 70 mL/min/1.73 m^2 using the Schwartz formula (Schwartz et al, J Peds 106:522, 1985) OR 24-hour Creatinine clearance or radioisotope GFR > 40 mL/min/m^2 or > 70 mL/min/1.73 m^2
- Shortening fraction of >27% by echocardiogram, or ejection fraction of >47% by radionuclide angiogram.

Stem Cell Infusion

Dosage/Timing

A minimum of 3 x 10^6 CD34 cells/kg (optimum 5 x 10^6 CD 34 cells/kg) PBSC should be used; or a minimum of 1.5 x 10^8 mononuclear bone marrow cells/kg (optimum > 2 x 10^8 cells/kg or > 8 x 10^4 CFU-GM/kg).

Stem cells will be infused intravenously on Day 0, 48 hours after chemotherapy is completed, immediately following thawing.

Toxicities

Toxicities may include an anaphylactic reaction, respiratory difficulty, hypotension, and volume overload. Other transfusions should be avoided if possible on the day of the stem cell infusion. Furosemide should be administered if clinically indicated.

Premedications/Monitoring

a) Premedications for hematopoietic progenitor cells infusion should be followed per each institutional guideline.
b) Ambu bag, Benadryl and epinephrine at bedside.
c) Place patient on cardiac monitor during infusion and for 1-2 hours following completion.