

TESTIS CANCER

RISK OF SECOND CANCERS IN SEMINOMA PATIENTS TREATED WITH XRT*

- **2,703 survivors of CSI seminoma from UK and Norway treated with infradiaphragmatic XRT**
- **Median F/U was 18 years**
- **385 second cancers were reported in 354 men; mainly gastric, pancreas, and bladder**
- **The excess of second cancers was statistically significant (IR 1.31; 95% C.I. 1.2-1.5)**
- **“Infradiaphragmatic XRT is associated with a significant excess of second cancers; policies for treating stage I seminoma should be revised”**

***Horwich A, Fossa S, et al.: Proc ASCO 28:351, 2010**

RISK OF SECONDARY MALIGNANCIES IN TESTICULAR CANCER PATIENTS TREATED WITH XRT*

- **SEER database from 1973-2006 identified 8,590 treated with XRT**

	<u>XRT</u>	<u>No XRT</u>
Number	8,590	11,710
Leukemia/lymphoma	76 (0.9%)	63 (0.5%)
Bladder cancer	56 (0.7%)	43 (0.4%)

***Lewinshtein D, et al.: Proc ASCO 28:351, 2010**

THE MOST CURABLE METASTATIC CANCER

- **Testis cancer: Most curable**
- **Second most curable: second-line therapy testis cancer**
- **Third most curable: third-line therapy testis cancer**

SALVAGE THERAPY OPTIONS FOR CURABLE PATIENTS

- **High dose chemotherapy followed by peripheral blood stem cell transplant**
- **VeIP or TIP x 4**
- **Salvage surgery**

PITFALLS IN SALVAGE THERAPY

- **Elevated HCG or AFP as only evidence of relapse or progressive disease**
- **Plateau in decline of HCG**
- **Sanctuary sites**

SALVAGE CHEMOTHERAPY WITH PBSCT: RESULTS*

	<u>No. pts.</u>	<u>No cont. NED (%)</u>
Entire series	184	116 (63%); 104 > 2 yr. cont. NED
Currently NED	122 (66%)	(4 Tax+Gem and 2 surg)
Second-line Tx	135	94 (70%)
Third-line or later	49	22 (45%)
hCG > 1,000	22	14 (64%)
Seminoma	35	26 (74%)
Platinum refractory	40	18 (45%)

*Einhorn LH, et al.: NEJM 357:10-18, 2007

CONVENTIONAL VS. HIGH DOSE SALVAGE CHEMOTHERAPY*

- **Retrospective international evaluation of second-line chemotherapy in patients with prior cisplatin combination chemotherapy**
- **Total of 1,594 patients (773 received standard dose salvage chemotx and 821 high dose chemotx)**
- **Prognostic variables assessed and patients grouped into low, intermediate of high risk disease**

*** Lorch A, et al: Proc ASCO 28:345,2010**

CONVENTIONAL VS. HIGH DOSE SALVAGE CHEMOTHERAPY (cont'd)

	PFS		OS	
	Events	2 years	Deaths	5 years
All pts (n=1594)				
CDCT	572/773	27.8 %	423/773	40.8 %
HDCT	418/821	49.6 %	362/821	53.2 %
	p < 0.001		p < 0.001	
Very low risk (n=76)				
CDCT	16/37	58,4 %	13/37	64,5 %
HDCT	4/39	91,6 %	4/39	88,7 %
	p < 0.008		p < 0.007	
Low risk (n=257)				
CDCT	78/122	40.0 %	40/122	66,2 %
HDCT	50/135	64.3 %	45/135	64,5 %
	p < 0.001		p = 0.901	
Intermediate risk (n=646)				
CDCT	229/318	31.9 %	158/318	45,5 %
HDCT	156/328	53.5 %	129/328	58,3 %
	p < 0.001		p < 0.002	
High risk (n=351)				
CDCT	122/152	17.2 %	109/152	23,0 %
HDCT	131/199	33.3 %	123/199	35,2 %
	p < 0.001		p < 0.001	
Very high risk (n=105)				
CDCT	53/54	1.9	48/54	3,4 %
HDCT	39/51	22.0	33/51	27,0 %
	p < 0.001		p < 0.002	

SERUM hCG

- **Half-life 18-24 hrs. (surgery versus chemotx)**
- **Embryonal cell CA, chorioCA and some seminomas**
- **THC**
- **Large cell lung CA, melanoma, bladder CA, G.I primaries, or cross reactivity with LH**

SERUM AFP

- **Half-life 5 days (surgery versus chemotx)**
- **Yolk sac tumor or embryonal cell CA**
- **Liver disease, liver metastases, adenocarcinomas**

SERUM LDH

- **Non-specific – not a “tumor marker”**
- **Elevated in many conditions, including after Neupogen or Neulasta**
- **Intermediate: LDH 1.5 – 10 x ULN**
- **Advanced: LDH > 10 x ULN**
- **Should never use LDH as sole criteria for risk stratification**

SERUM TUMOR MARKERS – TESTIS CANCER

- **Diagnosis**
- **Follow-up after therapy**
- **Marker level at start of chemotx, not orchiectomy, for risk stratification**
- **Clinical stage I, but rising serum hCG or AFP**
- **Post BEP for advanced disease, rising marker(s), but decreasing radiographic lesions**
- **IHC hCG, and AFP for carcinoma primary unknown**
 - **CD117, PLAP, CD30 , Oct 3 and Oct 4, glypican 3**

“INTERNATIONAL GERM CELL CONSENSUS”

Advanced (14%)

Intermediate (26%)

- **PMNSGCT**
- **Non-pulm. visc mets**
- **AFP > 10,000**
- **HCG > 50,000**
- **LDH > 10XULN**

at start of chemo

- **seminoma with non- pulmonary visc mets**
- **AFP 1,000 to 10,000**
- **HCG 5,000 to 50,000**
- **LDH 1.5 to 10 x ULN**

at start of chemo

**Chemotx: BEP x 4
or VIP x 4**

**Chemotx: BEP x 4 or
BEP x 3 and EP x 1**

HIGH hCG LEVELS

Course 1	1,200,000 mIU/ml
Course 2	8,000
Course 3	750
Course 4	120
1 month later	55
2 months later	25
3 months later	< 3

MANAGEMENT STRATEGIES FOR PATIENTS WITH VERY HIGH (> 50,000) hCG LEVELS*

- **Retrospective review of 41 patients who presented to Indiana University from 1976-1996 with advanced disease (hCG > 50,000 +/- other advanced criteria)**
- **22 of 41 (54%) continuously NED; however, only 2 of 41 had a normal hCG at start of 4th and final course of chemotx**
 - **8 additional patients normalized hCG 1 month later and 7 of these 10 continuously NED**
- **31 patients still had elevated hCG 1 month post 4th course cisplatin combination chemotx; 15 of these 31 (48%) cont. NED despite no further chemotx**

***Zon R, et al.: JCO 16:1294-1297, 1998**