Is there a role for conventional-dose chemotherapy in relapsed germ cell tumors?

Luana Toledo Manhaes, Daniel Musse Gomes, Isabele Small, Luiz H. Araujo, Pedro Masson Domingues
Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil
Email: lulutma@gmail.com

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BACKGROUND

Patients with germ cell tumors (GCT) that relapse after first-line platinum-based chemotherapy can still be successfully rescued with second-line regimens. High-dose chemotherapy has shown favorable outcomes, and is a preferred option in most instances. Herein, we argued if conventional-dose chemotherapy (CDCT) could also be an alternative in selected patients.

METHODS

We performed a retrospective observational study, analyzing medical data of 57 GCT male patients treated with salvage chemotherapy after relapse to first-line platinum-based treatment from 2000 to 2015 at the Brazilian National Cancer Institute.

RESULTS

The median age was 28 years (range 15 to 49). 26 patients (46%) were Afro-Brazilian, 45 (79%) were non-seminoma, and 53 (93%) had primary testis tumors. 14 patients (25%) had bone, liver or brain metastasis at relapse, and in 35 (61%) the progression-free interval (PFI) after first-line was < 3months.

The International Prognostic Factors Study Group (IPFSG) risk classification at relapse for very-low/low, intermediate and high/very-high risk were 8 (14%), 25 (44%), 24 (42%), respectively.

Only four patients in this cohort received one HDCT, but only one cycle, where is considered inappropriate. The majority patients were submitted a CDCT, 90% with a usual protocols.

After second line 30 patients (52%) had a favorable response rate with negative markers, 9 patients (16%) had a complete or partial response with positive markers and 18 (32%) had a progression disease.

After a median follow-up of 8 years, the 2-year PFS was 30% (95% IC, 20 % to 45 %) and the 2-year overall survival (OS) was 34% (Figure 1) (95% IC, 23% to 49%). PFI < 3m after first-line (Figure 2) (HR 2,38; p<0,005) and AFP > 1000 at relapse (Figure 3) (HR 2,38, p<0,023) were negative prognostic factors for PFS and OS.

The 2-year PFS and OS (Figure 4) for IPFSG risk classification very-low/low, intermediate and high/very-high risk were 75% and 73%, 28% and 32%, 18% and 24%, respectively.

Table 1. Patients and characteristics

Characteristics	No. (%)
All cohort	57 (100)
Age [median]	28 (15-49)
Ethnicity	
Caucasian	31 (54)
Afro-Brazilian	26 (46)
Histology	
Non-seminoma	45 (79)
Seminoma	12 (2)
Primary site	
Testis	53 (93)
Mediastinum	3 (5)
Retroperitoneum	1 (2)
Stage (TNM)	
I-II	8 (14)
III	49 (86)
Initial IGCCCG risk	
Poor	14 (25)
Intermediate	19 (33)
High	24 (42)
First-Line chemotherapy	
BEP	49 (86)
EP	4 (7)
VIP	4 (7)
Response to first line treatment	
CR-NED, PRm- (FRR)	29 (51)
SD, PRm+	28 (49)
PD	2 (4)
Progression-free interval after first-line chemotherapy	
<3 months	35 (61)
>3 months	22 (39)
AFP (ng-ml)	
<1000	46 (81)
>1000	6 (10)
Normal	5 (9)
HCG (U-L)	
<1000	42 (74)
>1000	6 (10)
Normal	9 (16)
Response to second line treatment	
CR-NED, PRm- (FRR)	30 (52)
SD, PRm+	9 (16)
PD	18 (32)
Salvage chemotherapy regimes	
Carbo + paclitaxel	1 (2)
EP	1 (2)
Gemcitabine + paclitaxel	1 (2)
TIP	16 (28)
VeIP	28 (49)
VeIP + HDCT (1 cycle)	4 (7)
VIP	5 (8)
Etoposide (oral)	1 (2)
Risk per IPFSG	
Low (low + very-low)	8 (14)
Intermediate	25 (44)
High (high + very-high)	24 (42)

Abbreviations: BEP, Bleomycin -Etoposide-Cisplatin; EP, Etoposide-Cisplatin; VIP, Etoposide, Ifosfamide, Cisplatin; IGCCCG, International Germ Cell cancer Collaborative Group; CR-NED, complete radiological response ; PRm-, partial response and negative markers; PRm+, partial response and positive markers; SD, stable disease; PD, progressive disease; NPVM, nonpulmonary visceral metastasis; AFP, alpha-fetoprotein; HCG, human chorionic protein; FRR, favorable response rate TIP, paclitaxel, Ifosfamide, Cisplatin; VeIP, vinblastin, Ifosfamide, Cisplatin; HDCT, high-dose chemotherapy, IPFSG, International Prognostic Factors Study Group.

All cohort – OS 2 years: 0.345 IC95% (0.2399-0.495)

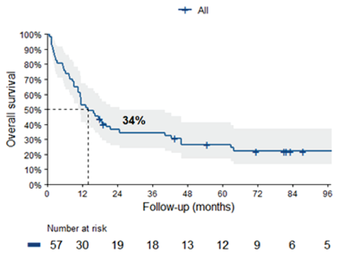

Figure 1 – Overall survival in 2 years

	median	Survival - 2y
PFI > 3 months	21.567	45%
PFI < 3 months	8.500	18%

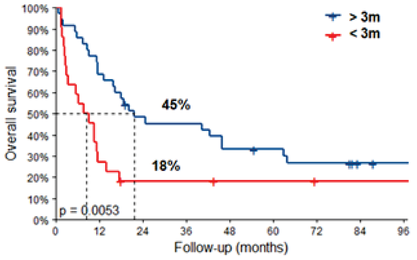

Figure 2 – Overall Survival stratified by PFI after first line

	median	Survival- 2y
AFP=<1000	16.467	38%
AFP=>1000	6.600	0%

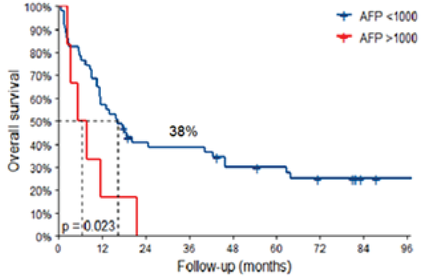

Figure 3 – Overall Survival Stratified by AFP

	median	Survival – 2y
Low risk (very low + low)	NA	72%
Intermediate risk	14.067	32%
High risk (high + very high)	9.967	24%

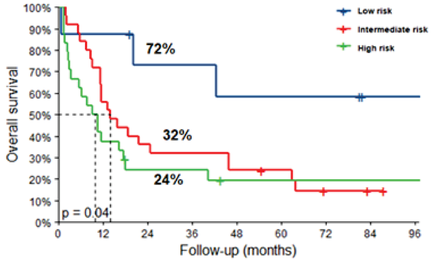

Figure 4 – Overall Survival stratified by Prognostic Score on recurrence

CONCLUSIONS

CDCT was associated with poor outcome in intermediate and high/very-high risk groups. However, in patients with relapsed GCT and very-low/low risk disease by the IPFSG classification, CDCT may be a reasonable option, achieving long-term survival rates. Further studies should be conducted to assess the best treatment in this subset, since even in second-line, many of patients are still potentially curable.

Projeto Gráfico: Área de Edição e Produção de Materiais Técnico-Científicos / INCA