



Discussion topic 2:
Therapy-refractory chronic GvHD case study

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Patient case: Presentation



Patient characteristics

Male, 35 years at HCT, ECOG 1, HCT-CI 1

Patient history prior to HCT

- AML ELN intermediate-1 diagnosed 28/01/2019
- Primary refractory to 3+7 and MIDAC
- Infectious complications: pansinusitis and proctitis
- Induction therapy with CLARA protocol
- Prolonged neutropenia
- Infectious complications: *C. diff.* colitis with sepsis
- Fecal microbiota transplantation from third party donor twice
- BM: CR 31/05/2019

Patient history: HCT

- Toxicity-reduced conditioning with FB3
- 10/10 HLA-identical unrelated donor: male, 29 years, B+, CMV+
- 8×10^6 CD34⁺/kg PBSC on 05/09/2019
- GvHD prophylaxis: ATG, CSA, and MMF
- Engraftment: ANC >500/ μ l Day +15, plts >20 000/ μ l Day +12
- Early complications: mucositis WHO 1 and neutropenic fever
- GvHD: Day +18 skin III, overall II; steroids at 2 mg/kg b.w.

Patient case: Presentation



Patient history: Early after HCT

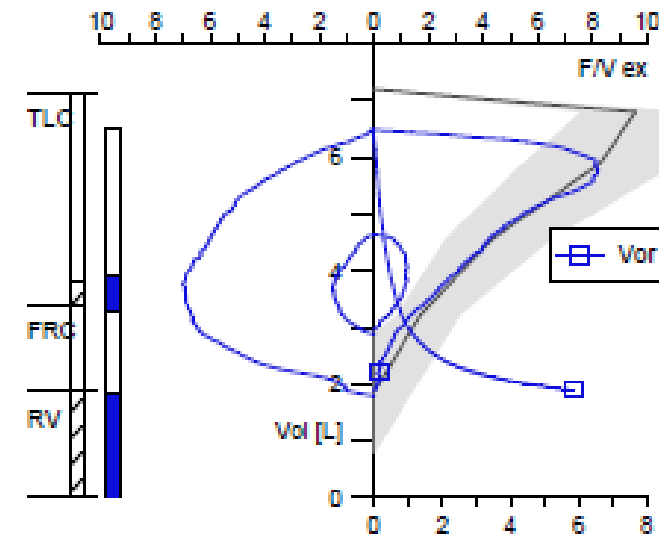
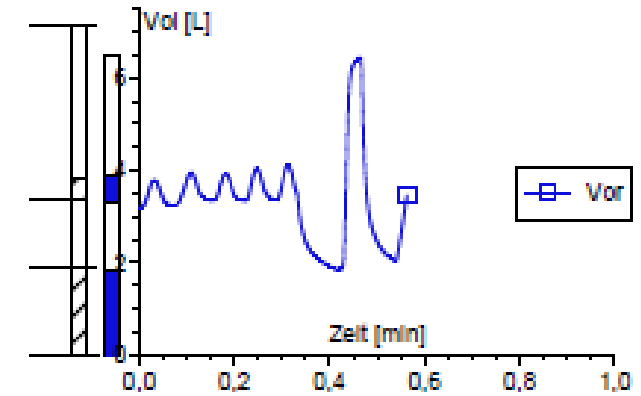
- BM Day +25: CR, complete donor chimerism
- *E. coli* ESBL colonization in anal region
- CMV infection: resolution after valganciclovir
- Polyoma BK cystitis
- Steroid diabetes

Patient history: Chronic GvHD

- Day +121: lichenoid oral mucosa
- Day +157 NIH-cGvHD score: skin 2, mouth 1, eyes 2, liver 2, genitals 1
- Platelets at 87 G/L

Pulmonary function test at Day +120

Substanz	I1				
	- nein				
	Soll	I1	%(I1/S)	Z	Z-Score
FVC	5.35	4.57	85	-1.21	●
FEV 1	4.35	3.47	80	-1.63	●
FEV 1 % FVC	81.62	75.88	93	-0.94	●
FEV 1 % VC...	81.62	74.49	91	-1.15	●
PEF	9.57	8.20	86	-1.14	●
MEF 75	8.23	6.74	82	-0.87	●
MEF 50	4.32	3.35	78	-0.87	●
MEF 25	1.71	0.92	54	-1.48	●
MIF 50		6.63			
PIF		7.03			
MIF		0.35			
VC IN	5.23	4.59	88	-1.15	●
VC MAX	5.35	4.65	87	-1.08	●
ERV	1.52	1.43	94		
TLC_SB	7.14	6.42	90	-1.03	●
RV_SB	1.87	1.80	96	-0.18	●
RV%TLC_SB	28	28	101	0.07	●
DLCOc_SB	10.68	8.96	84	-1.20	●
KCOc_SB	1.60	1.42	89	-0.86	●
VA_SB	6.70	6.29	94	-0.54	●
TA		10.8			



NIH Global Severity Scoring of cGvHD

Mild

- 1–2 organs (no lungs)
- Maximum organ score of 1

Moderate

- Three or more organs with max score of 1 OR
- **At least 1 organ (not lung) with max score of 2 OR**
- Lung score of 1

Severe

- At least 1 organ with score of 3 OR
- Lung score of 2 or 3

Indications for treatment of moderate/severe cGvHD



Systemic treatment indicated



Topical treatment may be added to speed up response, to improve response rate, and to spare systemic immunosuppression



Combination therapies may spare steroids but could interfere with GvL effect

Patient case: Presentation



Patient history: Early after HCT

- BM Day +25: CR, complete donor chimerism
- *E. coli* ESBL colonization in anal region
- CMV infection: resolution after valganciclovir
- Polyoma BK cystitis
- Steroid-diabetes

Patient history: Chronic GvHD

- Day +121: lichenoid oral mucosa
- Day +157: Skin 2, mouth 1, eyes 2, liver 2, genitals 1: moderate NIH-defined cGvHD
CsA, steroids at 0.5 mg/kg and ECP 2 days/2 weeks

Supportive care

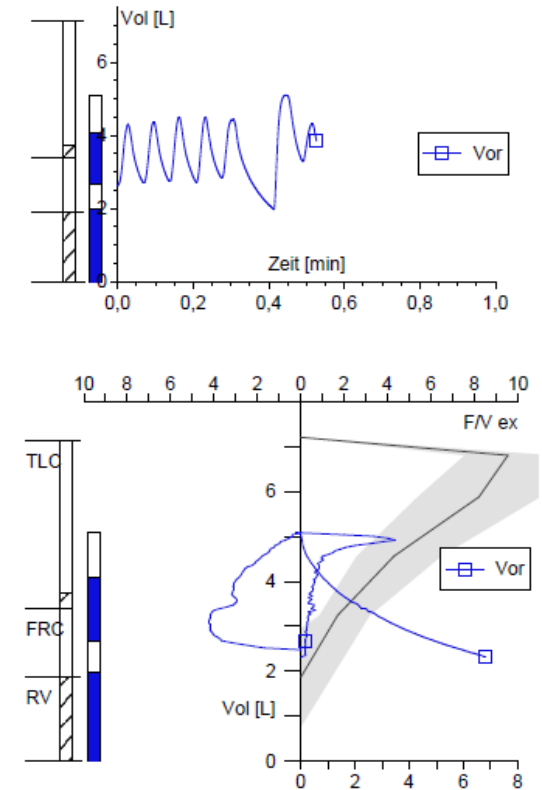
- Day +295: Eyes 2, ECP DC (CVC infection)
- Day +306: Steroids DC, CsA ongoing

Diagnosis of cGvHD of the lung

- What was the initial presentation of GvHD in the patient?
Dry cough, afebrile, no dyspnea on Day +325
- No other signs of cGvHD
- Immunosuppressive therapy with CsA ongoing, no steroids

	Soll	I1	%(I1/S)	Z	-3	-2	Z ₁ Score	2	3
FVC	5.34	2.73	51	-4.05					
FEV 1	4.33	1.10	25	-5.49					
FEV 1 % FVC	81.47	40.44	50	-4.67					
FEV 1 % VC...	81.47	35.28	43	-4.96					
PEF	9.53	4.36	46	-4.28					
MEF 75	8.20	0.78	10	-4.34					
MEF 50	4.29	0.30	7	-5.33					
MEF 25	1.68	0.21	13	-4.48					
MIF 50		3.14							
PIF		4.27							
MIF		1.02							
VC IN	5.20	3.13	60	-3.69					
VC MAX	5.34	3.13	59	-3.42					
ERV	1.51	0.71	47						
TLC_SB	7.14	5.08	71	-2.94					
RV_SB	1.89	1.99	105	0.23					
RV%TLC_SB	28	39	140	2.04					
DLCOcSB	10.64	6.63	62	-3.02					
KCOc_SB	1.60	1.33	83	-1.29					
VA_SB	6.70	4.98	74	-2.36					
TA		12.7							

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HR-CT scan at first decline of FEV1



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Diagnosis: Lung cGvHD

Diagnostic	Distinctive	Other	Common
Bronchiolitis obliterans diagnosed with lung biopsy	Air trapping and bronchiectasis on chest CT	Cryptogenic organizing pneumonia	
Restrictive lung disease			

PFTs recommended on Day +100, at initial diagnosis of cGvHD, at 1 year, and at 6-month intervals for first 2 years. More frequent PFTs in BOS patients.

If BOS is only clinical manifestation without prior diagnosis of cGvHD, **lung biopsy** is required for enrollment on general cGvHD trial.

NIH scoring: Lung cGvHD

	Score 0	Score 1	Score 2	Score 3
Symptom score	No symptoms	Mild symptoms <ul style="list-style-type: none">• Shortness of breath after climbing one flight of steps	Moderate symptoms <ul style="list-style-type: none">• Shortness of breath after walking on flat ground	Severe symptoms <ul style="list-style-type: none">• Shortness of breath at rest• Requiring O₂
Lung score: % FEV1	<ul style="list-style-type: none">• FEV1 \geq80%	<ul style="list-style-type: none">• FEV1 60–79%	<ul style="list-style-type: none">• FEV1 40–59%	<ul style="list-style-type: none">• FEV1 \leq39%

Diagnosis of cGvHD of the lung

- What was the initial presentation of GvHD in the patient?
 - Dry cough, afebrile, no dyspnoea on Day +325
- What diagnostic tests were performed?
 - PFT: severe obstruction, FEV1 25%
 - HR-CT scan: no air trapping, no bronchiectasis
 - BAL: no infection
 - Severity of cGvHD: severe

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