PONDEROSA

Observational study on CML patients in any phase treated with ponatinib (Iclusig®) at any dose.

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INTRODUCTION

Ponatinib is indicated for

- patients (pts) with chronic phase (CP), accelerated phase (AP) or blast crisis (BC) CML, with resistant or intolerant to prior tyrosine kinase inhibitors (TKIs) or with the bcr-abl mutation T315I

STUDY DESIGN

- German and czech multi-center, pro- and retrospective, non- interventional, observational study
- Inclusion of 100 adult CML pts in any phase treated with ponatinib at various dosages

OBJECTIVES

After 24 months of ponatinib treatment we considered:

1. **Assessment of OS and PFS**
2. **Incidence of AEs**
3. **Assessment of response to treatment**

OVERVIEW OF CENTERS

Fig. 1: Participating hematological centers

1ST INTERIM ANALYSIS

Status at time of data cut (July 2019)			
Patients (60 yrs. [21-89])		**Centers** (Fig. 1)	
Total	**51**	**Total**	**45**
- Pts on ponatinib	28	- Active centers	27
- Pts with ponatinib stop	23	- Initiated centers	18

- Initial ponatinib dose: 45mg/d (23 pts), 30mg/d (17 pts) and 15mg/d (11 pts)
- Dose reduction was observed in 18 pts, dose increase in 5 pts
- Median duration of ponatinib therapy was 16.8 months (0.33-49.6)

1. OS, PFS and patient outcome

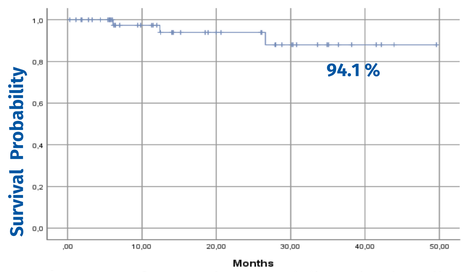

Fig. 2: OS of pts under ponatinib: 3 deaths; all CML-related (progression from CP)

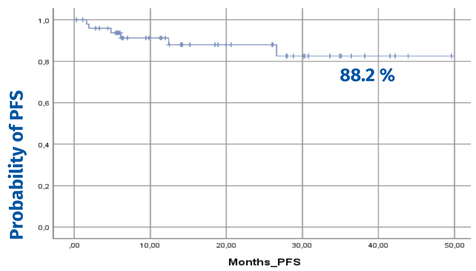

Fig. 3: PFS of pts under ponatinib: 4 pts progressed from CP to BC, 1 pt from CP to AP, 1 pt from AP to BC

- 3 pts were not in CP at ponatinib start:
  1 pt in BC: Allo-SCT (after 5.6 months); 2 pts in AP: 1 pt is still under ponat. with a current response of MR4, 1 pt progressed to BC
- 7 pts received Allo-SCT (median: 5.7 months after ponatinib start)

2. Adverse events

AEs in Ponderosa	Before Ponatinib; n (%)	After Ponatinib; n (%)	AEs in Ponderosa	Before Ponatinib; n (%)	After Ponatinib; n (%)
No. of pts with at least 1 AE	9 (18) #	33 (65)	No. of documented AEs (cont.):	15	135
No. of documented AEs:	**15 #**	**135**	**General disorders and conditions**	**n. d.**	**32 (24)**
Cardiac disorders	**5**	**6 (4.4)**	**Musculoskel.+connect. tissue disorders**	**n. d.**	**12 (8.9)**
Myocardial infarction	2	0			
Coronary heart disease	2	1 (0.7)			
others	1	5 (3.7)			
Vascular disorders	**9**	**8 (5.9)**	**Gastrointestinal disorders**	**n. d.**	**12 (8.9)**
Peripheral artery disease	1	0			
Hypertension	8	8 (5.9)			
Nervous system disorders	**1**	**15 (11)**	**Skin + subcut. tissue disorders**	**n. d.**	**10 (7.4)**
Ischemic Cerebrovasc. Disease	1	2 (1.5)	**Infections**		**7 (5.2)**
others	n. d.	13 (9.6)	**Respiratory, thoracic, mediast. disord.**		**6 (4.4)**
			Laboratory findings		**5(3.7)**
Blood and lymphatic system disorders	**n. d.**	**9 (6.7)**	**Injury/Inflammation/Deaths Neoplasms/Psychiat. disorders**	**n. d.**	**each 3 (2.2) each 2 (1.5)**

#: ***Note:*** **Not all categories of AEs are registered by anamnesis**

3. Response to treatment

- Assessment w/o 6 pts: 3 pts w/o any data of response and 3 pts were in BC/AP, s. Fig. 4 + *1.) OS, PFS and patient outcome*
- 26 achieved no MMR
- 17 pts achieved MMR, after a median of 6 months
- 2 pts were already in MMR at start

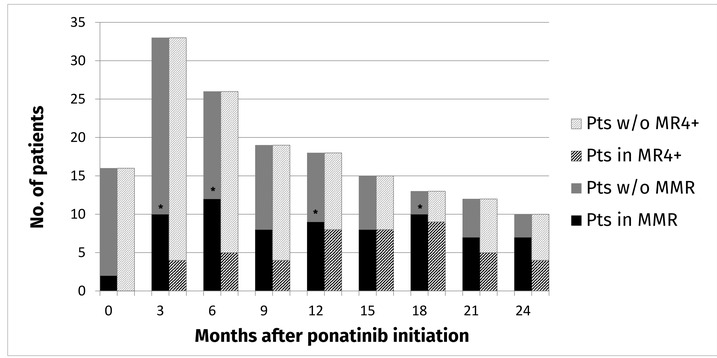

Fig. 4: Rates of MMR and MR4⁺ of patients in CP-CML at ponatinib start (n=45) during 24 months of therapy (3 pts with BC/AP at ponatinib start were excluded for MMR rate assessment and were separately observed, see, *1. OS, PFS and patient outcome*, **p≤0,05* MMR rate at each timepoint vs. MMR rate at 0 months (McNemar-Test)

- Nevertheless, the MMR rates increased at months 3, 6, 12 and 18 compared to MMR rate at ponatinib start (Fig. 4)

CONCLUSIONS

- This interim analysis shows first data of the real-life treatment with ponatinib in german and czech CML patients.
- All deaths (three) were caused by CML progression, not from a cardiovascular event.
- Progression was observed in 6 pts.
- AEs occurred in 65% of the pts.
- 11.8 % of the AEs were cardio-/cerebrovascular events.
- Although 50% of the pts in CP achieved no MMR under ponatinib therapy, the MMR rate increased over time after ponatinib initiation.

Zentrum für Klinische Studien

DEUTSCHE CML STUDIENGRUPPE

This observational study is conducted in collaboration with the German CML Study Group and with financial support of Incyte. Disclosure Clauß: I declare no conflict of interest.