HINC-207 – Pheno- and genotypes of JAK-2 mutated patients with and without thromboembolic events (OSHO #091)

Hennersdorf TF[1], Jaekel N[1], Tornow P[2], Kaempfe D[3], Spohn C[4], Moeller R[4], Ruessel J[5], Jentsch-Ullrich K[6], Schwarz M[7], Hurtz H-J[8], Boehme J[8], Schulze S[1], Al-Ali HK[1,2]

Polycythemia vera (PV) and essential thrombocytemia (ET) are classical *BCR-ABL* negative myeloproliferative neoplasms characterized by clonal expansion of myeloid cell lines. Thrombotic events are the main cause of morbidity and mortality in PV and ET. Several risk factors for thrombosis such as a hematocrit > 45%, older age, previous history of thrombosis, and the presence of the *JAK2* mutation have been identified. Yet, the pathogenesis of thrombotic events remains poorly understood. It is striking, that life-threatening thrombosis in absence of overt blood count abnormalities is common in younger patients. Thus, there is an unmet need to identify new potential phenotypical and genetic predictors of thrombosis risk in *JAK2*-mutated patients with PV and ET.

Methods and Design

HINC-207 (OSHO #091) is our prospective multicenter investigator-initiated project within the East German Study Group and financed by a grant from Novartis, Germany. Over a period of 24 months, 180 adult patients with *JAK2*-mutated PV and ET in 9 study centres will be enrolled and stratified according to the presence (Group A; n=60) or absence (Group B; n=120) of thrombotic events. After signed informed consent, exhaustive clinical data including disease-related risk factors and therapies, hereditary and acquired thrombophilic parameters as well as classical cardiovascular risk factors will be collected. In addition to the assessment of the *JAK2*-allel burden in the entire cohort, blood samples for the accompanying translational project for patients recruited at the University Hospital Halle who have signed the translational consent form will be stored. Data will be statistically analysed by the Institute for Medical Epidemiology, Biometrics and Informatics of the MLU. The independent effect of variables on thrombosis risk and the assumption of proportional hazards will be calculated by uni-/multivariate Cox proportional hazards model and the Schoenfeld residuals respectively.

Current Status and patient characteristics

At present, 8 sites have been activated. On 24/April/2019, the first patient signed informed consent. As of 22/November/2019, 206 patients have been recruited (Group A; n=59, Group B; n=147). Of these, 86 (42%) were males and 120 (58%) were females. There was no significant difference in gender distribution between the two groups. Disease was PV in 123 (60%) and ET in 75 (38%) patients. There were 2 cases each of post-PV-/post-ET-MF in group B (1%). Overall, disease distribution was similar in both groups.

With a median age of 65 (range 33-86) years, patients in group A were younger compared to patients in group B [median age was 68 (range 23-94) years]. 32 patients have signed informed consent for the concomitant translational project.

	A	B	total
total patients	59	147	206
PV (abs)	34	89	123
PV (%)	58	60	60
ET (abs)	25	54	79
ET (%)	42	37	38
MF (abs)	0	4	4
MF (%)	0	3	2
male	30	56	86
male (%)	51	38	42
female	29	91	120
female (%)	49	62	58

Tab.1: Currently available patient characteristics in both groups (as of 22/November/2019)

Presently, more extensive data has been collected on 31 patients, 17 of which had a thromboembolic event in their medical history, most frequently splanchnic vein thrombosis, strokes and deep vein thrombosis of the leg.

Conclusion and outlook

The extraordinary fast actual accrual of 24 patients per month as compared to the estimated 7.5 patients per month allows a completion of the entire study population by approximately 8 months instead of the planned 24 months per protocol. Accrual is expected to finish by the end of December, 2019. This allows data analysis to start in the second quarter of 2020.

The identification of potential phenotypical and genetic predictors of thrombosis risk in *JAK2*-mutated patients with PV and ET might improve treatment strategies and provide tools to prevent thromboembolic events in these patients.

1 Universitätsklinikum Halle, Departement Innere Medizin, Klinik für Innere Medizin IV Hämatologie, Onkologie und Hämostaseologie, Halle (Saale), 2 Krukenberg-Krebszentrum Halle, Halle (Saale), 3 Praxis für Hämatologie und Onkologie, ambulante Chemotherapie und Palliativmedizin, Lüdenscheid, 4 Hämatologisch-onkologische Gemeinschaftspraxis Halle, Halle (Saale), 5 Carl-von-Basedow-Klinikum Saalekreis gGmbH, Medizinische Klinik II Hämatologie – Onkologie/Palliativmedizin, Merseburg, 6 Schwerpunktpraxis für Hämatologie und Onkologie, Magdeburg, 7 Paracelsusklinik Adorf/Schöneck, Schwerpunktpraxis Onkologie und Hämatologie, Schöneck, 8 Gemeinschaftspraxis und Tagesklinik Innere Medizin, Hämatologie, Onkologie, Gastroenterologie und Palliativmedizin, Halle (Saale)