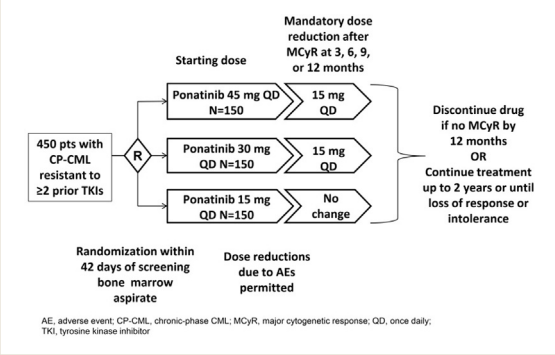
endpoints include rates of vascular occlusive events, AEs, and serious AEs.

Figure Study Schema



CML-066

Detection of BCR-ABL Kinase Domain Mutations in Chronic Myeloid Leukemia Patients

Nancy Escobar[*,1] Mariana Herrera,[1] Luisa Rosales,[1] Silvana Torselli,[2] Julio Caceres,[3] Mauricio Villegas,[1] Mariela Guerra,[1] Nely Marroquin,[1] Claudia Osorio,[1] Vanessa Zamora,[1] Darwin Alvarez,[1] Luis Alvarez,[1] Claudia Carranza[1]*

[1]*INVEGEM, Guatemala, Guatemala;* [2]*Roosevelt National Hospital, Guatemala, Guatemala;* [3]*San Juan de Dios National Hospital, Guatemala, Guatemala*

Context: The patient with chronic myeloid leukemia (CML) is treated successfully with tirosin kinase inhibitors (TKIs). Worldwide there are a 20 to 30% of patients, who have resistance to the treatment. The first cause of TKIs resistance is the presence of BCR-ABL kinase domain mutations. In Guatemalan population of around 35% of CML, patients are resistant to TKIs. **Objective:** In the present study, we propose the detection of the presence of BCR-ABL kinase domain mutations in the CML patients that have a resistance to the treatment with tirosin kinase inhibitors. **Design:** We analyzed 83 patients with CML that have treatment with TKIs for at least 18 months. These patients didn't achieved an optimal response. All of these patients had more than 1% in international scale (IS), this means that they didn't have complete cytogenetic response. We collected blood samples from patients. RNA was extracted from the peripheral blood, subsequently a RT-PCR and Sanger sequencing of the ABL domain kinase were performed. **Results:** We found that 11% of the patients analyzed have BCR-ABL kinase domain mutations. The most frequent mutation found in the Guatemalan population is G250E (6.1%), which is an aggressive P-loop domain mutation. The other mutations we detected in our population were T315I (1.2%), E279K (1.2%) and F359V (1.2%). In addition, we found one patient, with two mutations, the G250E and E453K. In **Table 1**, the patient sex, the TKIs, and the % IS, of all the patient with mutations, is shown. **Conclusion:** In conclusion, the frequency of BCR-ABL kinase domain mutation in the Guatemalan population is 11%; and the most frequent mutation is the G250E.

Table 1 Molecular and Clinical Characteristics of the Patients with Mutations

No.	Mutation	Sexo	TKI	%IS
1	G250E	M	Imatinib	38.374
2	G250E	M	Dastinib	68.37
3	G250E; E453K	M	Nilotinib	*
4	T315I	M	Nilotinib	3.84
5	E279K	F	Nilotinib	57.85
6	G250E	F	Imatinib	*
7	F359V	M	Dasatinib	33.1
8	G250E	F	Imatinib	1.43
9	G250E	M	Imatinib	95.03

* More BCR-ABL1 copies than ABL gene control.

CML-077

OPTIC-2L: a Superiority Trial of Two Lower Doses of Ponatinib Versus Standard Dose Nilotinib in Second-Line Chronic Phase CML

Jeffrey Lipton[*,1] Andreas Hochhaus,[2] Angelo Carella,[3] Marianne Severinsen,[4] Peter te Boekhorst,[5] Antonio Almeida,[6] Charles Chuah,[7] Violaine Havelange,[8] Gabriela Baerlocher,[9] Stephanie Lustgarten,[10] Heinrich Farin,[10] Frank Haluska[10]*

[1]*Princess Margaret Cancer Centre, Toronto, Canada;* [2]*Jena University Hospital, Jena, Germany;* [3]*Hematology and BMT Unit, IRCCS San Martino-IST, Genova, Italy;* [4]*Aalborg University Hospital, Aalborg, Denmark;* [5]*Erasmus Medical Center, Rotterdam, Netherlands;* [6]*Portuguese Institute of Oncology of Lisbon, Lisbon, Portugal;* [7]*Singapore General Hospital and Duke-NUS Medical School, Singapore, Singapore;* [8]*Cliniques universitaires Saint-Luc and de Duve Institute Université Catholique de Louvain, Brussels, Belgium;* [9]*Inselspital/ University Hospital Bern, Bern, Switzerland;* [10]*ARIAD Pharmaceuticals, Inc., Cambridge, MA, United States*

Context: Up to half of chronic-phase chronic myeloid leukemia (CP-CML) patients with first-line tyrosine kinase inhibitor (TKI) imatinib treatment become resistant or intolerant. A sizable portion of patients (38-49%) do not achieve major cytogenetic response (MCyR) with second-line treatment with dasatinib, nilotinib, or bosutinib. None of these agents have activity against all known kinase domain mutations and all are refractory to the T315I mutation. Ponatinib (45 mg daily), a potent pan-BCR-ABL TKI, demonstrated strong efficacy among a small cohort of second-line CP-CML patients, including those with the T315I mutation, in the pivotal PACE trial (NCT01207440). Longer follow-up of the overall study population revealed a higher incidence of arterial