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Background

Comorbid conditions, including solid and hematologic malignancies, may impact risk of contracting SARS CoV-2 or having severe COVID-19. Data specific to individual cancer types is essential to differentiate impact of patient, disease, and therapy specific factors on risk and outcomes, as the pandemic remains uncontrolled.

Goal
The primary goal of the CANDID study was to rapidly collect and analyze information on COVID-19 cases among CML pts to define prognosis, risk factors and outcome. Defining risk and predisposing features in CML patients could guide interventions, therapy modifications, and clinical management for patients and physicians.

**Methods**

From March 12, 2020, the iCMLf sent an anonymized case collection form to its global network of physicians treating CML pts and partner organizations. Forms were reviewed and cases tracked by an iCMLf data manager. Updates were provided weekly. Only confirmed cases or those with high level of suspicion were collected. Denominators regarding affected cohort (% tested, % affected in CML population) were not available in most instances.

**Results**

As of July 1, 2020, 110 cases of COVID-19 were reported to iCMLf from 20 countries: 61% from Europe, 15% from Asia, 12% from South America, 10% from North America, 2% from Africa and 1% from Oceania. COVID-19 was diagnosed by PCR and/or serology in 93 pts (85%) and clinically suspected in 17 pts (15%). Forty-six physicians reported 91 of the CML pts with COVID-19 out of a total of 12,236 CML pts that they were following (0.7%).

Median age at the time of COVID-19 diagnosis was 54 years (range: 18-89) and 55% of pts were males. Median time from CML diagnosis to COVID-19 was 7 years (range: 0-25). CML treatment at the time of COVID-19 diagnosis consisted of hydroxyurea in 1 pt (1%) and TKI in 77 (70%). Five (5%) pts were taking bosutinib, 12 (11%) dasatinib, 39 (36%) imatinib, 17 (16%), nilotinib, 2 (2%) ponatinib, 1 (1%) HQP1315 and 1 pt (1%) was treated with an unknown TKI. Eighteen (16%) pts were untreated at the time of COVID-19 diagnosis, 8 due to elective treatment discontinuation (TFR) and 10 for other reasons (toxicity (5), stem cell transplantation (1), unknown (1) and newly diagnosed CML (3)). CML treatment information was lacking at the time of cut-off in 14 cases (13%). Thirty-three (30%) cases were reported as having interrupted TKI therapy during COVID-19.

From 110 reports COVID-19 was asymptomatic in 8 cases (7%). In the 102 symptomatic pts (93%), COVID-19 was considered as mild (no hospitalization) in 49 cases (45%), moderate (hospitalization) in 19 cases (17%), severe (intensive care) in 19 cases (17%) and of unknown severity in 15 cases (14%). At the data cut-off date, COVID-19 was still active in 14 pts (13%) and outcome was unknown in 9 pts (8%). Among the 87 others, outcome was favorable in 75 pts (86%) and fatal in 12 (14%).
We analyzed overall survival in the 87 patients with known outcome according to sex, age, CML duration, type of CML treatment, line of TKI therapy, history of smoking, comorbidities, TKI interruption due to COVID-19, administration of any treatment against COVID-19 (antimicrobial agents, steroids, oxygen or anti-IL-6 antibodies) and economic status of country. Univariate analysis identified older age (75 vs < 75 years; mortality rate: 60% vs 7%, p<0.001), severity of COVID-19 (severe v non-severe; mortality 63% vs 0%, p<0.001) and imatinib treatment (mortality: imatinib 25% vs 2nd gen TKI 3% vs no TKI 0%, p=0.003) as predictors for COVID-19 mortality (Figure 1). Notably, 25% of imatinib treated patients were over 75 years old, compared to none of the patients treated with second generation TKI.

**Conclusion**

The CANDID study represents the largest global cohort study to date characterizing COVID-19 in CML. Currently, the mortality rate from COVID-19 in evaluable CML patients is 13.7%. Factors associated with a higher mortality rate are age and imatinib therapy. Imatinib may represent a confounder as opposed to a true adverse prognostic predictor given the strong link between imatinib treatment and advanced age. Further case reports and longer follow up are needed to better ascertain independent risk factors, the impact of COVID-19, and the possible role that TKI type may play in this population.

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A.  

|                   | Total | Mortality rate (%) | Patients who survived | Patients who died | p-value |
|-------------------|-------|--------------------|-----------------------|-------------------|---------|
| Age < 75 years    | 20    | 80%                | 16 (80%)              | 4 (20%)           | 0.0003  |
| Age ≥ 75 years    | 32    | 76%                | 28 (87.5%)            | 4 (12.5%)         |        |
| Sex               | Female | 30 | 100% | 26 (86.7%) | 4 (13.3%) | 0.0003  |
| Sex               | Male   | 62 | 100% | 44 (71%)   | 18 (28.8%) | 0.0003  |
| Race              | Caucasian | 50 | 100% | 43 (86%)   | 7 (14%)    | 0.0003  |
| Race              | Non-Caucasian | 32 | 100% | 27 (84.4%) | 5 (15.6%) | 0.0003  |
| Length of time with CML | < 5 years | 21 | 64% | 16 (76.2%) | 5 (23.8%) | 0.07 |
| Length of time with CML | 5-19 years | 32 | 66% | 21 (65.6%) | 11 (34.4%) | 0.67 |
| History of Cancer | No     | 41 | 84% | 32 (78.0%) | 9 (22.0%) | 0.0003  |
| History of Cancer | Yes    | 56 | 15% | 56 (100%)  | 0 (0%)     | 0.0003  |
| Cardiac problems | No     | 47 | 100% | 41 (87.2%) | 6 (12.8%) | 0.47 |
| Cardiac problems | Yes    | 42 | 100% | 37 (88.1%) | 5 (11.9%) | 0.47 |
| Bi-intervention due to COVID-19 diagnosis | No | 36 | 7% | 20 (55.6%) | 16 (44.4%) | 0.65 |
| Bi-intervention due to COVID-19 diagnosis | Yes | 16 | 100% | 16 (100%) | 0 (0%) | 0.65 |
| COVID-19 mortality | No     | 54 | 5% | 54 (100%)  | 0 (0%)     | 0.64 |
| COVID-19 mortality | Yes    | 2 | 50% | 1 (50%)    | 1 (50%)    | 0.64 |
| Dynamic status of invasity | No | 54 | 5% | 54 (100%)  | 0 (0%)     | 0.34 |
| Dynamic status of invasity | Yes | 2 | 50% | 1 (50%)    | 1 (50%)    | 0.34 |
| Upper cytoplasm | No     | 11 | 100% | 11 (100%)  | 0 (0%)     | 0.13 |
| Upper cytoplasm | Yes    | 3 | 33% | 1 (33.3%)  | 2 (66.7%)  | 0.13 |
| Lower cytoplasm | No     | 8 | 16% | 5 (62.5%)  | 3 (37.5%)  | 0.16 |
| Lower cytoplasm | Yes    | 2 | 33% | 1 (33.3%)  | 1 (66.7%)  | 0.16 |
| Treatment at time of COVID-19 diagnosis | No | 54 | 5% | 54 (100%)  | 0 (0%)     | 0.003 |
| Treatment at time of COVID-19 diagnosis | Yes | 2 | 50% | 1 (50%)    | 1 (50%)    | 0.003 |
| Status of COVID-19 | No | 54 | 5% | 54 (100%)  | 0 (0%)     | 0.88 |
| Status of COVID-19 | Yes | 2 | 50% | 1 (50%)    | 1 (50%)    | 0.88 |

B.  

- 49 years, 94%, n=33  
- 50-64 years, 88%, n=21  
- ≥75 years, 50%, n=8

p=0.0021

C.  

- Imatinib  
- Next-gen TKI  
- Other therapy  
- No TKI

p=0.03

p=0.33

Figure 1. The impact of risk factors for mortality in CML patient with COVID-19. (A). Univariate analysis determining risk factors of death in CML patients with COVID-19. p-value was derived from Fisher's exact test. (B). Kaplan-Meier survival plot comparing survival among the age groups. p-value was derived from log-rank test. (C). Boxplot shows the age against treatment group at the time of COVID-19 diagnosis. p-value was derived from Mann-Whitney test. Red colour boxplot represents patients who died and green colour boxplot represents patients who survived groups.

Disclosures

**Rea:** Incyte: Honoraria, Membership on an entity's Board of Directors or advisory committees; Pfizer: Honoraria, Membership on an entity's Board of Directors or advisory committees; BMS: Membership on an entity's Board of Directors or advisory committees; Novartis: Honoraria, Membership on an entity's Board of Directors or advisory committees. **Mauro:** Bristol-Myers Squibb: Consultancy, Honoraria, Other: Travel, Accommodation, Expenses, Research Funding; Pfizer: Consultancy, Honoraria, Other: Travel, Accommodation, Expenses, Research Funding; Sun Pharma/SPARC: Research Funding; Novartis: Consultancy, Honoraria, Other: Travel, Accommodation, Expenses, Research Funding; Takeda: Consultancy, Honoraria, Other: Travel, Accommodation, Expenses, Research Funding.

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Author notes
* Asterisk with author names denotes non-ASH members.

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