



Changes in Stem Cell Transplant activity and procedures during SARS-CoV2 pandemic in Italy: an Italian Bone Marrow Transplant Group (GITMO) nationwide analysis (TransCOVID-19 Survey)

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Abstract

The Transplant Centers belonging to Gruppo Italiano per il Trapianto di Midollo Osseo (GITMO) conducted a survey with the aim of evaluating the effect of SARS-CoV2 pandemic on the allogeneic transplant activity in Italy. The pandemic period from 1/3/2020 to 31/7/2020 was compared with the same period in 2019. Overall, in 2020 there was a 2.4% reduction in the number of allo-HCT cases compared to 2019. Interestingly, this deflection did not affect the acute leukemia cases (+5.7% in 2020). The use of peripheral blood-derived stem cells (+10.7%) and cryopreservation (97.4% of the centers) was highly adopted in 2020. Despite the sanitary emergency, almost all of the surveyed centers declared no impact of SARS-CoV2 pandemic on the transplant timing and outcomes, and the sanitary policy was positively evaluated by the majority of centers. The emergency measures ensured that only a minority of the allo-HCT patients had been infected by SARS-CoV2; however, a mortality of 42.1% among the allo-HCT patients hospitalized for COVID-19 was recorded. This survey gives us the information that the GITMO Group reacted positively to the pandemic. Thanks to the emergency strategies, the Italian allo-HCT activity continued safely, showing only a minor deflection and offering the same probability of cure to the transplanted patients.

The SARS-CoV2 pandemic dramatically affected the health activities. In Italy, as well as in the majority of the Countries, efforts have been made to guarantee treatments for acute and

oncological patients. This is the case of onco-hematological patients submitted or candidate to allogeneic hematopoietic stem cell transplantation (allo-HCT) [1]. Starting from 24th February, 2020, date on which the first COVID-19-positive patient has been identified in Italy, decrees and recommendations have been released by the National and International Health Authorities in order to provide adequate medical assistance to hematological and transplant patients [2] (<http://www.salute.gov.it/portale/home.html>, <https://www.ebmt.org/covid-19-and-bmt>, <https://www.siematologia.it/files/COVID19-Raccomandazioni-SIE-GITMO.pdf>,

Members of the GITMO Centers are listed above reference list.

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Table 1 Comparison of transplant characteristics between March–July 2019 and March–July 2020.

	2019 N°	2020 N°	Variation N°	%
Number of allo-HCT, <i>n</i> (%)	462	451	−11	−2.4
Disease:				
Acute Leukemia (AML & ALL)	281	297	+16	+5.7
Myelodysplastic Syndrome	41	40	−1	−2.4
Myeloproliferative Neoplasms	35	33	−2	−5.7
Hodgkin Lymphoma	14	13	−1	−7.1
Non-Hodgkin Lymphoma	41	26	−15	−36.6
Multiple Myeloma	12	9	−3	−25.0
Non-neoplastic hematological diseases	38	34	−4	−10.5
Oncological neoplasia	0	1	+1	NA
Type of Donor:				
Sibling	108	112	+4	+3.7
Unrelated Donor	218	216	−2	−0.9
Haploidentical	127	116	−11	−8.6
Cord Blood	9	9	0	0
Source HSC:				
Peripheral Blood	339	376	+37	+10.0
Bone Marrow	114	66	−48	−42.1
Cord Blood	9	9	0	0
Number of unrelated donor searches	405	412	+7	+1.7
Shift from Foreign to Italian Donor	1	16	+15	+1500
Donor IC withdrawal	4	10	+6	+150
Frontline Haplo transplant	33	37	+4	+12.1
Unrelated Donor not available	4	12	+8	+200

IC informed consent, NA not available.

http://www.ptpl.altervista.org/burl/2020/burl_33_2020_ddg_06082020_9583.pdf, <https://www.ebmt.org/sites/default/files/2020-03/EBMT%20COVID-19%20guidelines%20v.3.2%20%282020-03-16%29.pdf>). The most relevant ones allowed the transfer of a donor search from the international to the national bank registry (IBMDR) and the possibility to cryopreserve hematopoietic stem cells (HSCs), when there was concern that the donor was at high risk of community-acquired infection between work-up and collection (Supplementary Table 1).

On behalf of Gruppo Italiano per il Trapianto di Midollo Osseo (GITMO), we designed a specific Survey (TransCOVID-19 Survey), consisting of 40 multiple choices questions in order to investigate the effects of SARS-CoV2 pandemic on the Italian Transplant Centers activity. The

first pandemic wave (from March 2020 the 1st to July 2020 the 31st) was compared to the same period of the year 2019. Five different items were investigated: (I) the transplant activity in terms of numbers and characteristics of transplant procedures; (II) the opinion of Centers regarding transplant outcome in COVID-19 era; (III) the number of subjects infected by SARS-CoV2 virus among allo-HCT patients and staff personnel; (IV) the future transplant perspectives, and (V) the grade of satisfaction about the National and International recommendations.

The survey was completed by a total of 39/47 (83.0%) allogeneic transplant Centers, with 100% valid answers. In addition, eight GITMO-affiliated autologous transplant Centers sent information on the total number of autologous transplant procedures in order to evaluate the impact of the pandemic in the autologous setting. Overall, they declared 51 auto-transplant in 2020 compared to 60 in 2019 (−15% decrease). No more analyses were carried out in auto-transplant category (Supplementary Tables 2 and 3a–e).

Taking into account the Italian allo-HCT activity, there was only a mild decline in the numbers of allo-HCT compared to the same period of the previous year (−2.4%) (Table 1). Interestingly, the reduction mostly affected less aggressive diseases, such as lymphoma and myeloma, as well as autologous procedures, while an increase in the number of allo-HCT for acute leukemias (+5.7%) was even observed. The reason for this observation may be well-explained by the different allo-HCT urgency of such diseases [3, 4]. The effect of SARS-CoV2 pandemic did not apparently impact on the algorithm of donor' choice. Indeed, in the large majority of cases, the Centers did not change their donor selection policies: sibling, unrelated, haploidentical and cord blood stem cell source distribution slightly changed during the pandemic. Nevertheless, more frontline haploidentical donors were reported and a higher proportion of unrelated donors (UD) refused to donate for potential donation-related infectious risk. In order to maintain the donor selection and transplant standards, while ensuring the safety of patients undergoing conditioning therapy in case of unexpected donor unavailability, more UD were recruited by IBMDR and a significant increase in the use of peripheral blood-derived stem cells (PBSC) (+10.9%) and PBSC cryopreservation (employed in 38 [97.4%] in 2020 vs 19 Centers [48.7%] in 2019) was observed, as recommended by the Health Authorities [5, 6].

Besides the raw numbers of transplant procedures, 23 centers (59.0%) retained that SARS-CoV2 pandemic had no impact on transplant timing, while only 2 Centers (5.1%) declared mild to significant reduction of transplant timing and 14 (35.9%) an increase in the interval from the first patient evaluation to transplant. Altogether, these observations may reflect the efforts of allo-HCT transplant Centers

to guarantee the transplant continuity. In doing so, whilst in 2019 almost all Center (35/39, 89.7%) did not use telemedicine, 31 centers (79.5%) declared telemedicine employment during the pandemic: notably, in 14 out of 31 centers (45.2%) telemedicine was extended to $\geq 25\%$ of ambulatory visits. Moreover, in the opinion of the large majority of the interviewed Centers, there was no effect of the pandemic on the transplant-related outcomes.

Eighteen allo-HCT Centers (46.2%) managed hematological patients with COVID-19. The rate of hematological SARS-CoV2 positive patients was generally low (1–9 cases for 88.9% of involved Centers). However, among the hospitalized allo-HCT SARS-CoV2-positive patients the mortality rate was particularly high (8 cases out of 19, 42.1%). In 9 Transplant Centers (23.1%) personnel redistribution was requested to provide assistance to non-hematologic SARS-CoV2-positive patients. Regarding SARS-CoV2-infected personnel, 22 Centers (56.4%) referred staff members to be infected by SARS-CoV2 virus, for a total of 79 individuals. Seven out of 79 subjects (8.9%) required hospitalization in three centers (7.7%) with no fatalities. The isolation measures well limited the spread of the infection among allo-HCT patients. Nevertheless, the virus confirmed its severe impact on immune-depressed patients, with a mortality higher than 40% among the hospitalized transplant subjects, as recently reported by an Italian multicenter study [7]. Also, SARS-CoV2 pandemic had a significant impact on the staff personnel too, highlighting once again the psychological and physical implications of the pandemic among the hospital professionals.

The latter part of the survey relied on possible transplant perspectives after the end of SARS-CoV2 crisis. For 28 Centers (71.8%), an extended PBSC utilization could be maintained or even increased in the early future; on the contrary, PBSC cryopreservation was expected to return to pre-SARS-CoV2 era by 16 (41.0%) Centers, while 13 Centers (33.3%) and 10 Centers (25.6%) foresaw only a mild decrease or stabilization. For 28 (71.8%) Centers the preferential use of Nationals donors compared to foreign donors will be maintained (15, 38.5%) or even increased (13, 33.3%). A total 16 Centers (41.0%) predicted a stabilization or increase in the use of telemedicine, while 12 (30.8%) and 11 (28.2%) Centers hypothesized a slight or significant reduction, respectively.

Finally, the Centers reported a positive judgement of indications and recommendations provided by Italian and European Health Authorities; overall, as confirmed by the first Survey's section, the recommendations effectively guided the Italian transplant activity by all the surveyed Centers.

What is going to remain after this experience in the future? The opinion poll considered the emergency measures as the cryopreservation of HSCs, the use of telemedicine useful but temporary in the majority of cases.

Long-term analyses are required to confirm the safety and efficacy of such approach in normal clinical practice.

In conclusion, this survey suggests that collaborative network between Health Authorities, Scientific Societies and Transplant Centers ensured to continue a safe transplant activity among GITMO-affiliated Centers.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interest.

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