## SGLT-2 inhibitor-related polycythemia – from the Dubrava University Hospital Registry

Tomislav Čikara<sup>\*</sup>,
Marko Lucijanić,
Marin Pavlov,
Irzal Hadžibegović,
Nikola Pavlović,
Šime Manola,
Ivana Jurin

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\*ADDRESS FOR CORRESPONDENCE: Tomislav Čikara, Klinička bolnica Dubrava, Av. G. Šuška 6, HR-10000 Zagreb, Croatia. / Phone: +385-95-804-5968 / E-mail: t.cikara@gmail.com

**ORCID:** Tomislav Čikara, https://orcid.org/0000-0001-8012-4481 • Marko Lucijanić, https://orcid.org/0000-0003-3962-2774 Marin Pavlov, https://orcid.org/0000-0003-3962-2774 • Irzal Hadžibegović, https://orcid.org/0000-0002-3768-9134 Nikola Pavlović, https://orcid.org/0000-0001-9187-7681 • Šime Manola, https://orcid.org/0000-0001-6444-2674 Ivana Jurin, https://orcid.org/0000-0002-2637-9691

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**Introduction**: Sodium-glucose co-transporter 2 (SGLT-2) inhibitors are the latest addition to guidelinedirected medical therapy in heart failure (HF)<sup>1</sup>. It has been documented that SGLT-2 inhibitors significantly increase hemoglobin (Hgb) and hematocrit (Hct) levels via several supposed mechanisms<sup>2</sup>.



FIGURE 1. Dynamics of secondary polycythemia in a heart failure patients over t and 12 months of follow-up. SP = secondary polycythemia We analyzed SGLT-2 inhibitors treated HF patients and dynamics of Hgb and Hct levels in follow-up period of 12 months.

**Metods**: We consider all of patients with or developing Hgb levels >160 g/L for females or >165 g/L for males to represent secondary polycythemia (SP).

Patients and Results: We analyzed a total of 848 SGLT-2 inhibitor treated HF patients. At the baseline, median Hgb was 136 g/L, IQR (124-147). A total of 31 (3.7%) patients fulfilled WHO criteria for polycythemia. At 6 months, median Hgb was 140 g/L, IQR (127-150) and was significantly higher in comparison to baseline (P<0.001). At 12 month, median Hgb was 141 g/L, IQR (130-151) and was significantly different in comparison to baseline (P<0.001) but not in comparison to 6 months (P=0.253). Percentage of patients with SP did not significantly differ at 6 months (5.2%) and 12 months (3.5%) in comparison to baseline (P>0.05 for both analyses). However, structure of the patient cohort presenting with SP significantly differed over time (P<0.001) as shown in Figure 1. About 1% of patients had persistent SP at both 6 months in comparison to baseline and at 12 months in comparison to

baseline and 6 months milestone. However, during first 6 months 4% of patients developed de-novo SP in comparison to baseline, whereas 2% of patients experienced SP resolution. At subsequent 6 months, 3% of new patients developed SP and 3% of new patients experienced SP resolution in comparison to first 6 months period. Overall, during 12 months similar proportion of patients developed SP and experienced SP resolution, whereas 1% of patients had persisting SP.

**Conclusion**: These observations shed novel light on phenomenon of erythrocytosis developing in association with SGLT-2 inhibitor use in HF patients. As our data show, there is continuous exchange of patients who develop and resolute SP over time with only a fraction of them (1%) experiencing persistent polycythemia, and therefore probably require further hematologic workup.

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