INTRODUCTION
• Globally, incidence of chronic myeloid leukemia (CML) accounts for 10 to 15 patients per 1,000,000 population per year4.
• Adherence to CML medications has been reported to be suboptimal.
• Non-adherence to CML therapies can lead to substantial clinical burden; however, data pertaining to economic implications of non-adherence is scarce.
• We have, therefore, conducted a systematic review to assess the cost implications of non-adherence to treatment among the patients with CML.

RESULTS
• A total of six out of 216 screened studies were included in the literature review.
• All the six studies were observational-retrospective in design.
• Mean age of the included patients ranged from 48.5 years5 to 54 years6 as reported in three studies.
• Of the six studies, four studies were conducted in the US, while one study each was conducted in Italy and Taiwan.
• Adherence to treatment was measured using medication possession ratio (MPR) in five of the six studies, while one study measured the adherence using proportion of days covered (PDC).
• The majority of studies assessed non-adherence to imatinib only (four studies), while two studies assessed adherence to dasatinib, imatinib, and nilotinib7-8.
• Variation in cut-offs to measure non-adherence was observed, ranging from MPR<65% to MPR<85%.
• The percentage of non-adherent patients to imatinib ranged from 20% (MPR<50%) to 66% (MPR<85%) (Figure 1).
• Study by Esposti and colleagues comparing tyrosine-kinase inhibitors suggested that non-adherence (PDC<80%) was highest among patients receiving nilotinib (54%) when compared with imatinib (22%) and dasatinib (14%) (Figure 1). Further, study by Hsieh and colleagues reported that 14% patients were non-adherent (MPR<48%) to dasatinib, imatinib, or nilotinib (Figure 1).

US
• Patients who were adherent to imatinib (MPR45%) throughout their observation period (up to 3 years) incurred lower average cost of treatment per quarter compared to the patients who were not always adherent to imatinib (MPR45%) ($11,759 vs. $13,773). Further, 3-year extrapolation results reported that per patient healthcare costs were $24,168 less for patients who were adherent at each of the study quarters compared to non-adherent patients.
• Patients non-adherent to imatinib (MPR45%) were associated with a statistically significant higher total cost of care (p<0.03), inpatient costs (p<0.001), non-imatinib pharmacy costs (p<0.001), and outpatient costs (p=0.001) when compared with adherent patients with good adherence to imatinib (MPR>70%) as reported in a 12-month study (Figure 2).
• Additionally, mean total medical costs and total healthcare costs with good adherence to imatinib (MPR70%) were 77.3% ($121,247) and 29.9% ($37,264) less as compared to poor adherence to imatinib with MPR<85% during entire follow-up period (mean follow up: 2.5 years), respectively.

RESULTS
• Total healthcare costs per person over the 12-month follow-up period were also highest among patients with low MPR receiving imatinib (<50%) ($US131,357), followed by intermediate MPR (50%-90%) ($US54,770), high (90%-95%) ($US35,236), and very high MPR (>95%) ($US42,250) (Figure 3).

ITALY
• Leukemia-related hospitalizations costs for a follow-up period of 6 months were also reported to be higher in non-adherent patients (PDC<40%) compared to adherent patients (PDC≥80%) (average cost per patient: $567 vs. $54).

TAIWAN
• Hsieh et al reported a statistically significantly higher adjusted inpatient cost per person year in interruption vs persistence group ($US5,674 vs. $US2,642; p<0.001) and non-adherence versus adherence group ($US4,390 vs. $US2,260; p<0.001). On the other hand, adjusted outpatient cost per person year was reported to be higher in persistence group compared to interruption group ($US31,443 vs. $US22,071; p<0.001) and adherence group compared to non-adherent group ($US30,295 vs. $US18,259; p<0.001).

METHODS
• Systematic search of Excerpta Medica database (Embase®) and Medical Literature Analysis and Retrieval System Online (MEDLINE®) databases was conducted to identify relevant studies assessing the impact of non-adherence to CML medications on the related healthcare costs.
• Inclusion criteria: English language studies published post 2005 and assessing non-adherence and its economic impact among adult patients (≥18 years) with CML.
• Data were extracted from the relevant studies by two independent reviewers with any discrepancy resolved by a third independent reviewer.

REFERENCES

CONCLUSIONS
• Findings of the current review suggested that non-adherence to CML therapies is associated with higher total healthcare cost including medical, inpatient, and outpatient cost.
• Thus, improvement in adherence is required to decrease the total healthcare cost and thereby, the economic burden among patients with CML.