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Ibrutinib can be effective even at the lowest dose after 10 years of treatment

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THIS CASE DEMONSTRATES THE EFFICACY OF THE LOWEST IBRUTINIB DOSE FROM THE BEGINNING AND CONTINUOUS TREATMENT FOR MORE THAN 10 YEARS IN RELAPSED / REFRACTORY CLL PATIENT WITH MINIMAL ADVERSE EFFECTS.

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INTRODUCTION

AFTER THE FIRST APPROVAL OF IBRUTINIB IN 2013 FOR THE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL), IT HAS BEEN EVIDENT THAT BRUTON TYROSINE KINASE INHIBITORS WILL CHANGE THE TREATMENT PARADIGM IN CLL.

FIVE-YEAR FOLLOW-UP STUDIES OF IBRUTINIB HAVE SHOWN IMPRESSIVE RESULTS WITH A 92% PROGRESSION-FREE SURVIVAL (PFS) AND OVERALL SURVIVAL (OS) WHEN USED AS FIRST LINE AND 43% PFS, 57% OS WHEN USED IN RELAPSED-REFRACTORY CLL.

THE DISCONTINUATION RATES WERE MORE THAN 30% AT 5 YEARS DUE TO DISEASE PROGRESSION AND MORE THAN 20 % DUE TO IBRUTINIB INTOLERANCE.

WITH A MEDIAN FOLLOW-UP OF NEARLY 10 YEARS, A MEDIAN PFS FOR MAJORITY OF PATIENTS IS MORE THAN 85 MONTHS, BUT LOWER IN RELAPSED/REFRACTORY PATIENTS (UP TO 49 MONTHS).
IN CASE OF INTOLERANCE OR ADVERSE EVENT, IBRUTINIB DOSE CAN BE REDUCED AND SEVERAL STUDIES HAVE SHOWN THAT PATIENTS WHO REDUCED THE DOSE REMAINED ON IBRUTINIB LONGER COMPARED WITH THOSE WHO DID NOT HAVE THE DOSE REDUCED.

CASE PRESENTATION

A 52-YEAR OLD MALE HAS BEEN DIAGNOSED WITH CLL IN 2005. AT THE TIME, HE WAS ASYMPTOMATIC, RAI 1, BINET B, CLL IPI LOW RISK SO HE WAS MONITORED WITHOUT TREATMENT.
IN 3 YEARS HE STARTED TO DEVELOP GRADUAL SYMPTOMS, INCLUDING INTERMITTENT FEVER, INCREASING FATIGUE, LOSS OF APPETITE, AND WEIGHT LOSS. ON EXAM, HE WAS FOUND TO HAVE INCREASING LYMPHADENOPATHY AND LYMPHOCYTOSIS. FISH WAS REPEATED AND DIDN'T SHOW ANY ABNORMALITIES. AFTER DISCUSSION OF TREATMENT OPTIONS, HE RECEIVED 3 CYCLES OF FLUDARABINE, CYCLOPHOSPHAMIDE (FC) AND PREDNISONE WITH COMPLETE REGRESSION OF LYMPHADENOPATHY AND LYMPHOCYTOSIS BUT PROLONGED NEUTROPENIA. AFTER 2 YEARS, HE PROGRESSED AND FC WITH RITUXIMAB WAS ADMINISTERED FOR 3 CYCLES. DUE TO PERSISTENT LYMPHADENOPATHY, THE TREATMENT CONTINUED WITH CYCLOPHOSPHAMIDE, VINCRISTINE, PREDNISONE AND RITUXIMAB (COP-R) FOR 3 CYCLES BUT WITH PARTIAL RESPONSE.
IN 2 YEARS HE PROGRESSED AGAIN AND RECEIVED ADDITIONAL 3 CYCLES OF R-COEP, BUT THE DISEASE WAS REFRACTORY TO TREATMENT.
IN MAY 2015. THE PATIENT STARTED TREATMENT WITH IBRUTINIB IN A COMPASSIONATE USE PROGRAM.
AT START OF TREATMENT HE WAS RAI STAGE IV WITH BULKY LYMPHADENOPATHY. DUE TO INCREASED LIVER ENZYMES, HEPATITIS B SEROLOGICAL TESTING WAS DONE AND SHOWED PARAMETERS FOR IMMUNITY FOLLOWING INFECTION, WHILE HBV-DNA WAS NEGATIVE. BECAUSE HBSAG POSITIVITY WAS CONSIDERED AS AN EXCLUSION CRITERION IN IBRUTINIB CLINICAL TRIALS, NO RECOMMENDATION WAS PROVIDED IN GUIDELINES FOR THE MANAGEMENT OF PAST HBV INFECTION.
THE PATIENT STARTED ANTIVIRAL PROPHYLAXIS AND INITIAL IBRUTINIB DOSE OF 140MG DAILY. AFTER 6 MONTHS OF IBRUTINIB TREATMENT, HIS LYMPHADENOPATHY RESOLVED FOR MORE THAN 50%. AFTER 12 MONTHS OF TREATMENT, THE PATIENT ACHIEVED COMPLETE REMISSION AND HAS CONTINUED WITH DAILY DOSE OF 140MG IBRUTINIB FOR THE NEXT 10 YEARS . IBRUTINIB HAS BEEN WELL TOLERATED WITHOUT SIGNIFICANT ADVERSE EVENTS AND GREAT QUALITY OF LIFE.

CONCLUSION

THE FIRST DOSE REDUCTION OF IBRUTINIB IN R/R CLL PATIENTS IN REAL-WORLD SETTINGS WAS OFTEN REPORTED DURING THE FIRST YEAR OF TREATMENT. DOSE MODIFICATIONS WERE MAINLY ATTRIBUTED TO TOXICITY, BUT THE PATIENTS WHO HAD AT LEAST A DOSE REDUCTION HAD A SIMILAR PFS THAN PATIENTS WITH NO DOSE REDUCTION, CONFIRMING THE THEORY THAT IBRUTINIB CAN STILL BE ADMINISTRATED IN CASE OF ADVERSE EVENTS WHILE KEEPING CLL UNDER CONTROL.

THIS CASE DEMONSTRATES THE EFFICACY OF THE LOWEST IBRUTINIB DOSE FROM THE BEGINNING OF TREATMENT AND DURING THE NEXT 10 YEARS OF TREATMENT IN RELAPSED / REFRACTORY CLL PATIENT WITH MINIMAL ADVERSE EVENTS.

PREVIOUS HBV INFECTION SHOULD NOT BE A CONTRAINDICATION FOR TREATING CLL PATIENTS WITH IBRUTINIB OR OTHER SIGNAL INHIBITORS, BUT REGULAR FOLLOW UP AND ANTIVIRAL PROPHYLAXIS ARE NEEDED WHEN THERE IS A RISK OF REACTIVATION.

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DISCLOSURES
NO DISCLOSURES