Justification
Patients of type 2 diabetes mellitus (T2DM) have two physiologic defects—
a) Impairment of insulin action on different target tissues (insulin resistance) and
b) Inadequate or abnormal insulin secretion from pancreatic β-cell (β-cell dysfunction)\textsuperscript{31}.

Generalized belief and scientifically proved that insulin resistance (IR) is
the primary and initial event that forced the β-cell to secret more insulin to
overcome hyperglycemia. It is β-cell dysfunction which unable to secret
required insulin (β-cell failure) leads to development of impaired glucose
tolerance and ultimately T2DM. Treatment initiated to reduce the risk of
insulin resistance by non-pharmacological management like patients
education, dietary regulation, regular physical exercise, reduction of body
weight (obesity), and lifestyle modification. Later insulin secretagogues
like sulfonylurea and incretin mimetics (physiologic secretagogues) are
used. Increased demand of insulin in T2DM due to insulin resistance (IR),
progressive reduction of β-cell mass (assumed to be, along with other
causes, genetically determined), and functional defect of β-cell (β-cell
dysfunction) makes secretagogues is of no use for prolonged period.
Sulfonylurea might cause increased arrhythmic cardiovascular events
particularly in large doses. Secretagogues increases the secretion of
insulin as well as co-packaged amylin consequently from β cell.
Accumulation of amylin in islets, though not fully proved, might contribute
to the late failure of insulin production with long standing t2dm. IR followed by overproduction of insulin follow the course. Insulin sensitizers have multifaceted action. They improve insulin action, reduce IR as well as insulin demand, might improve β-cell function, delayed the β-cell mass loss and take care of associated dislipidemia. Nowadays insulin sensitizers (IS) get a primary place for the treatment of t2dm. IS are of two types-a) biguanides like Metfomin and b) thiazolidinedione like pioglitazone. Metformin (MET) is commonly used, safe, effective, well efficacious, low cost antidiabetic agent with versatile pharmacological action and worldwide long standing experience drug. Precise mechanism of action is still unknown. Pioglitazone has well known mechanism of action, improve glycemic control both in monotherapy and combination therapy, good efficacious drug and has β-cell protective action. But it has adverse effect like hepatopathy, weight gain (not desirable in t2dm), anaemia, bone fracture. So the use of sulfonylurea and IS together improve glycemic control and to some improve β-cell function even may delay the progressive loss. Which is the better IS in combination therapy? Still remain unanswered. So far my knowledge there is no such head to head trial on this matter. Therefore a study is required to find out the comparative efficacy of metformin and pioglitazone both in monotherapy and combination therapy with glibenclamide/insulin in t2dm patients.