STATINS- CURRENT STATUS
&
FUTURE OUTLOOK

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FLOW OF PRESENTATION

- Objective of the study
- Secondary Research
- Statin Market scenario
- Primary Research
- Key Findings
- Suggestions

RESEARCH OBJECTIVES

OBJECTIVES

1. To assess market and find out the current status of Statin therapy
2. To determine the future trends in statin therapy

SUB OBJECTIVES

1. Comparative analysis of 2 most prescribed statins:

   a) Atorvastatin b) Rosuvastatin

2.Comparison of 2 statins based on

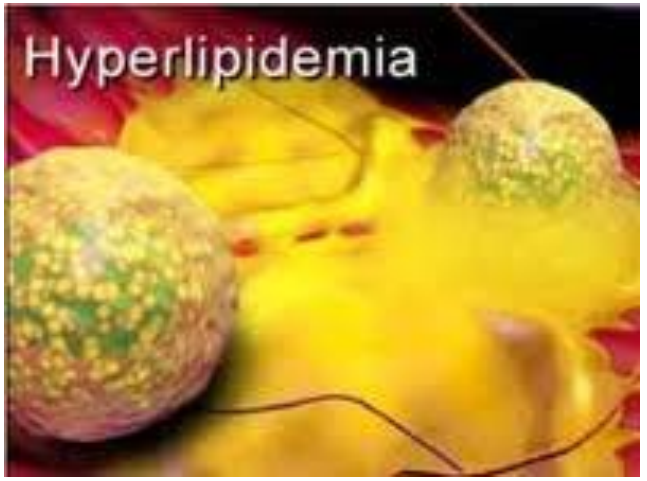
   a) Preference
   b) Choice for diabetic patients
   c) In primary prevention of CVD and strength preferred for achieving LDL-C goals
   d) Major advantages and drawbacks

3. Determine the preference of doctor for monotherapy and combination therapy of statins based on LDL-C goals

4. Find out the unmet needs of statins and the suggested options to satisfy those unmet needs

SECONDARY RESEARCH

& THEIR FINDINGS



DISEASE OVERVIEW

HYPERLIPIDEMIA : DESCRIPTION

- Hyperlipidemia is a medical condition that is characterized by excessive amounts of fatty substances such as cholesterol and triglycerides in the blood of an individual.
- Hyperlipidemia is often also known as hyperlipoproteinemia as fatty substances are often found attached to the proteins in the bloodstream. These increased levels of proteins and lipids often slow down the body's metabolic process by blocking various veins and arteries and can be very fatal if left unchecked.
- High lipid levels can speed up a process called atherosclerosis. Atherosclerosis leads to the blocking of arteries through formation of plaque.

Source- www.healthscout.com/ency/68/366/main.html

- High lipid level causes serious health complications including
  - Coronary artery diseases
  - Acute MI
  - Stroke
  - Diabetes
- Desirable lipid levels are as follows.
  - LDL less than 130 mg/dL or < 70 if you have established diagnosis of diabetes
  - HDL greater than 40 mg/dL (men) or 50 mg/dL (women);
  - Total cholesterol less than 200 mg/dL; and
  - Triglycerides less than 200 mg/dL or 150 if you have established heart disease or diabetes

Source- NCEP ATP III classification of cholesterol

PATHOPHYSIOLOGY OF HYPERLIPIDEMIA

- Cholesterol: essential for cell membrane formation & hormone synthesis
- Lipids not present in free form in plasma; circulate as lipoproteins
- 3 major plasma lipoproteins:
  - **VLDL** carries ~10 to 15 % of total serum cholesterol; carried in circulation as TG; VLDL = TG/5
  - **LDL** carries 60 to 70% of total serum cholesterol; IDL is also included in this group
  - **HDL** carries 20 to 30% of total serum cholesterol; reverse transportation of cholesterol
- VLDL secreted from the liver is converted to IDL then LDL
- Plasma LDL taken up by receptors on liver, adrenal, & peripheral cells

Source- Cha-23, Pharmacotherapy: A Pathophysiologic Approach The McGraw-Hill Companies

TYPES OF HYPERLIPOPROTEINEMIA

- Hyperlipidemia (elevation of cholesterol levels and/or triglyceride levels) has been defined by the Fredrickson classification, which is based on a beta-quantification, a process involving ultracentrifugation followed by electrophoresis.

Hyperlipoproteinemia	Increased lipoprotein	Defect	Treatments
Type I	Chylomicrons	Decresed lipoprotein lipase or altered Apo-C2	Diet control
Type IIa	LDL	LDL receptor deficiency	Statins, Bile acid sequestrants,niacin
Type IIb	LDL & VLDL	Decreased LDl receptor & increased apo-B	Statins, Niacin, Fibrates
Type III	IDL	Defect in Apo-E2 synthesis	Statins, Fibrates
Type IV	VLDL	Increased VLDL production.	Statins, Niacin, Fibrates
Type V	VLDL and Chylomicrons	Increased VLDL production.	Niacin, Fibrate.

RISK FACTORS OF HYPERLIPIDEMIA

Age	• Men: 45 years • Women: 55 years or premature menopause without estrogen replacement therapy
Family history of CVD	• Definite myocardial infarction or sudden death before age 55 years in father or other male first-degree relative, or before age 65 years in mother or other female first-degree relative
Hypertension	• 140/90 mm Hg or taking antihypertensive medication
Low level of HDL	• <40 mg/dL

Risk factor cont.....

obesity	• Higher weight leads to the grater risk of developing hyperlipidemia
Sedentary lifestyle	• Sedentary lifestyle leads to the higher lipid level.
Uncontrolled diet	• Diet containing higher level of fat and lipids is a major risk factor for developing the hyperlipidemia.

NCEP ATP III guidelines

TREATMENTS AVAILABLE

FOR HYPERLIPIDEMIA

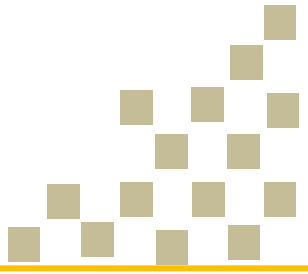
TREATMENTS OF HYPERLIPIDEMIA

- Initial treatment of hyperlipidemia includes dietary changes, weight reduction and exercise. If lifestyle modification is not sufficient for achieving optimal lipid levels then drug treatment should be considered.
- Major drug class used in treatment of hyperlipidemia are as follows.

1) Statins
2) Fibrates
3) Niacin
4) Bile acid sequestering resins
5) Cholesterol absorption inhibitors.

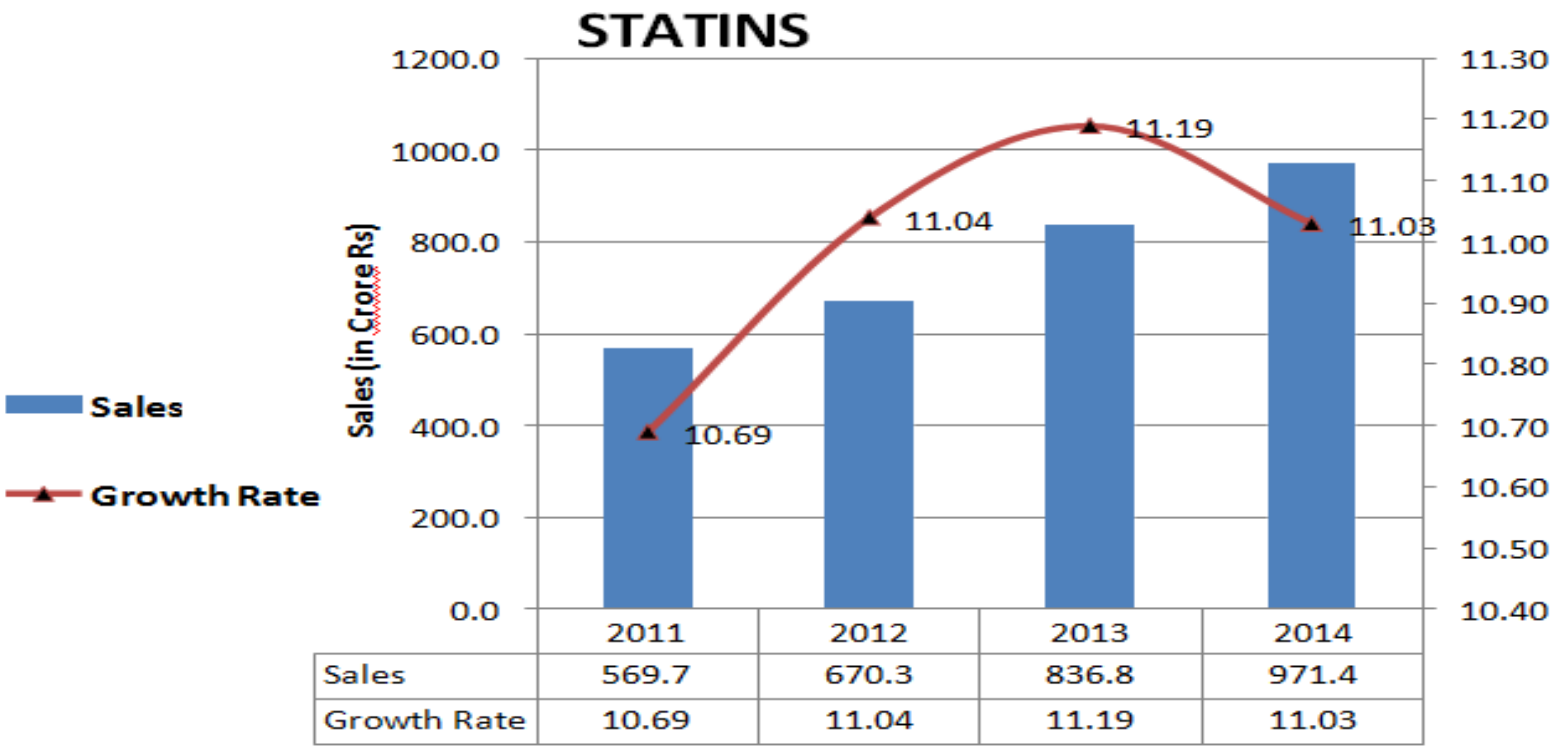
Attributes	Rosuvastatin	Atorvastatin
potency	High	low
Absolute bioavailability	20%	12%
Protein binding	88%	98%
Volume of distribution	134 L	565 L
Metabolism	Minimal hepatic metabolism. Metabolized by CYP450 2C9.	Hydrolyzed by liver (CYP450 3A4)
Excretion	Feces(90%) Urine(10%)	Feces (98%) Urine (2%)
Half-life	19 hours	14 hours
Effect on kidney	Damaging	Protecting
Cost of Therapy	High	Low

MARKET SCENARIO



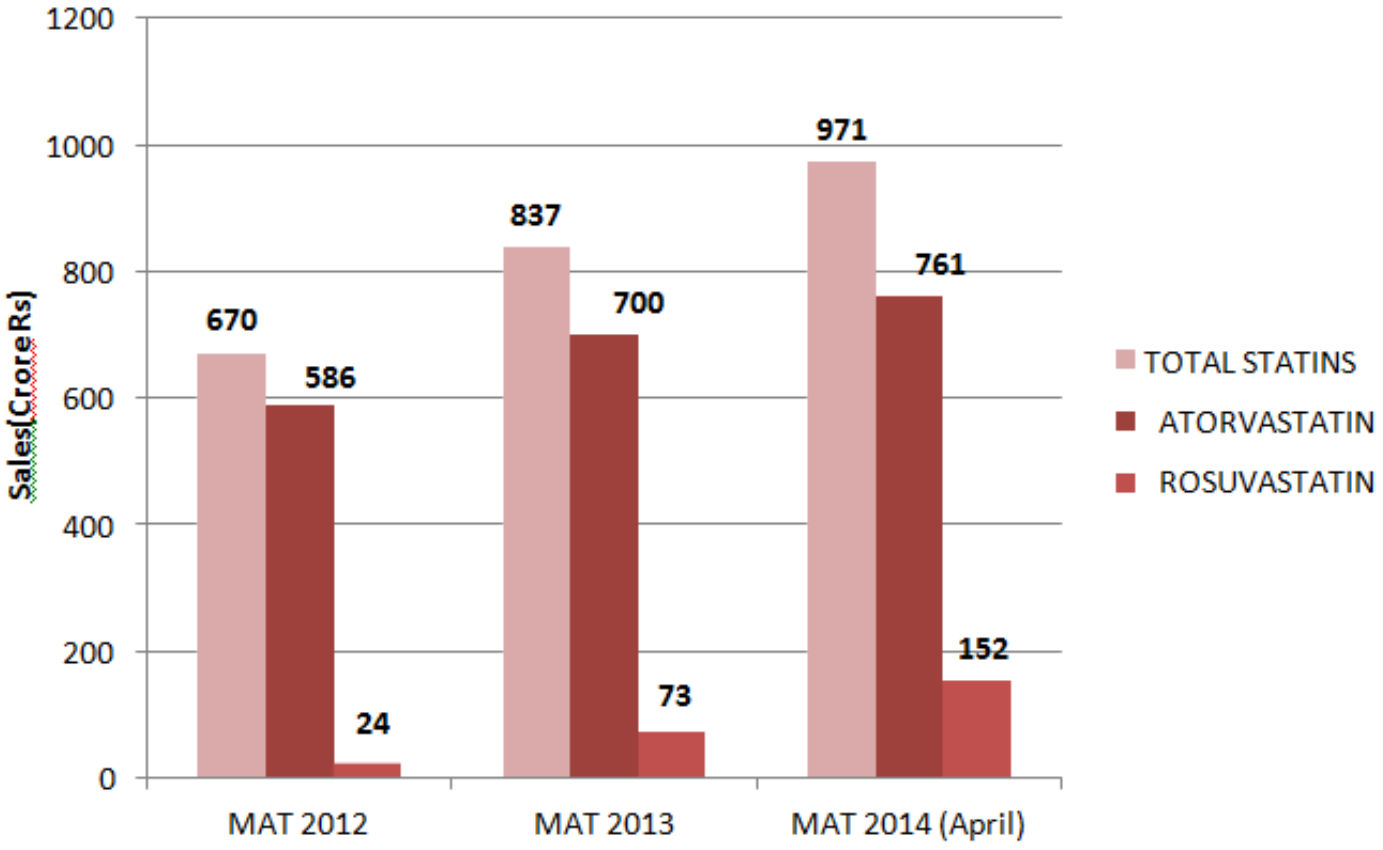
STATIN MARKET: SALES SCENARIO

- Total statin market is growing year by year with a CAGR (2011-2014) of 14.27%.
- Total sales of statins are also increasing at a tremendous rate.

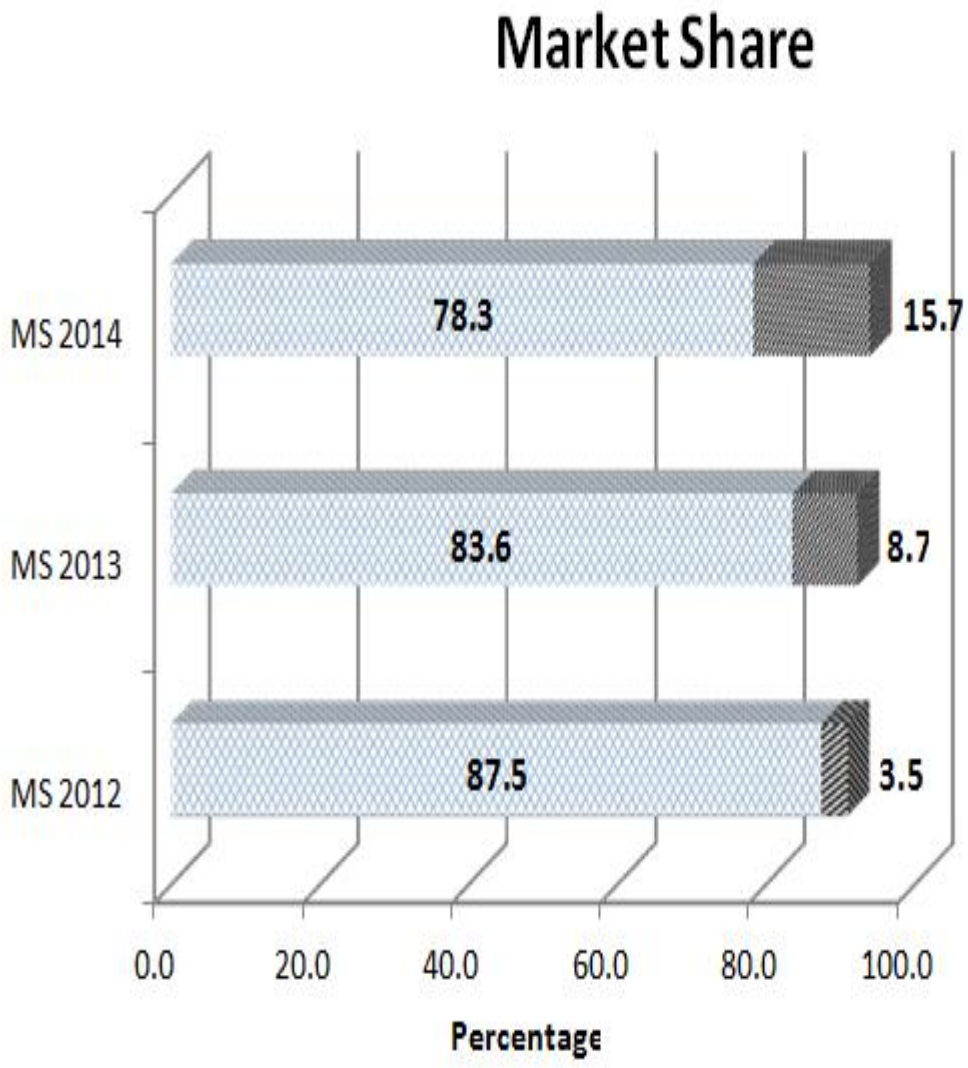


	2011	2012	2013	2014
Sales	569.7	670.3	836.8	971.4
Growth Rate	10.69	11.04	11.19	11.03

COMPARISON OF ATORVASTATIN & ROSUVASTATIN



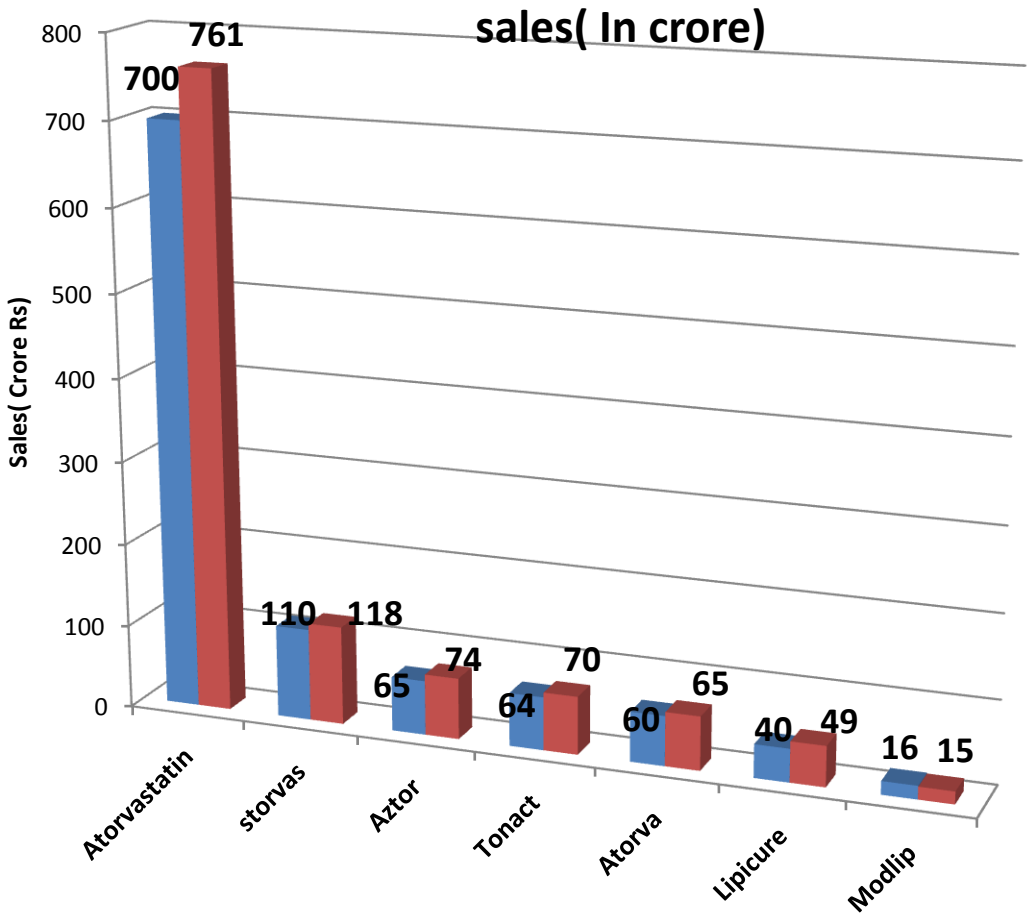
- Atorvastatin constitute the most of the statin market however Rosuvastatin sales is increasing at tremendous rate



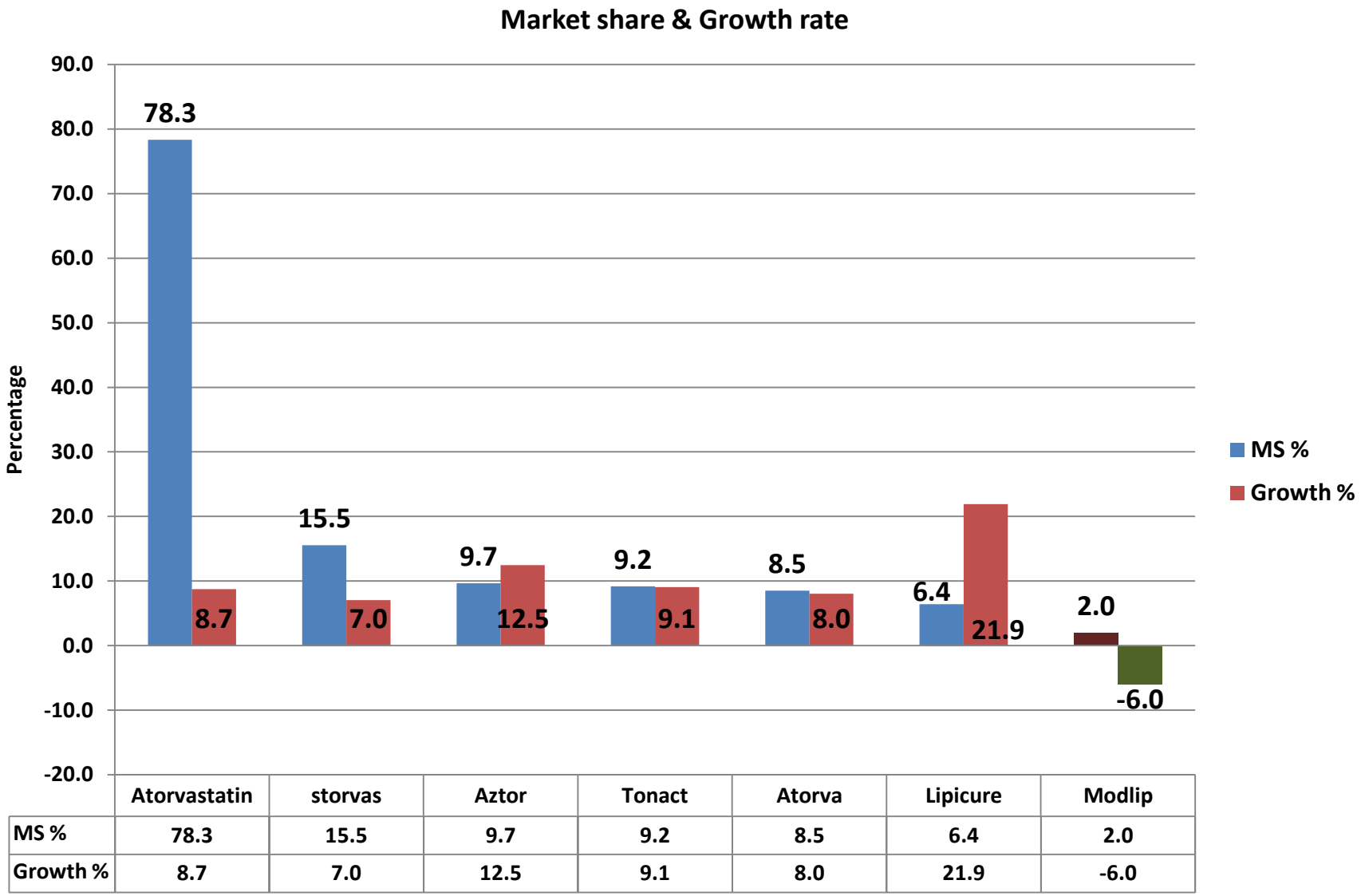
- Atorvastatin market share and growth rate both decreases over the years.
- Rosuvastatin market share and growth rate increases at higher rate.

*All Figures in percentage%

ATORVASTATIN BRANDS SALES

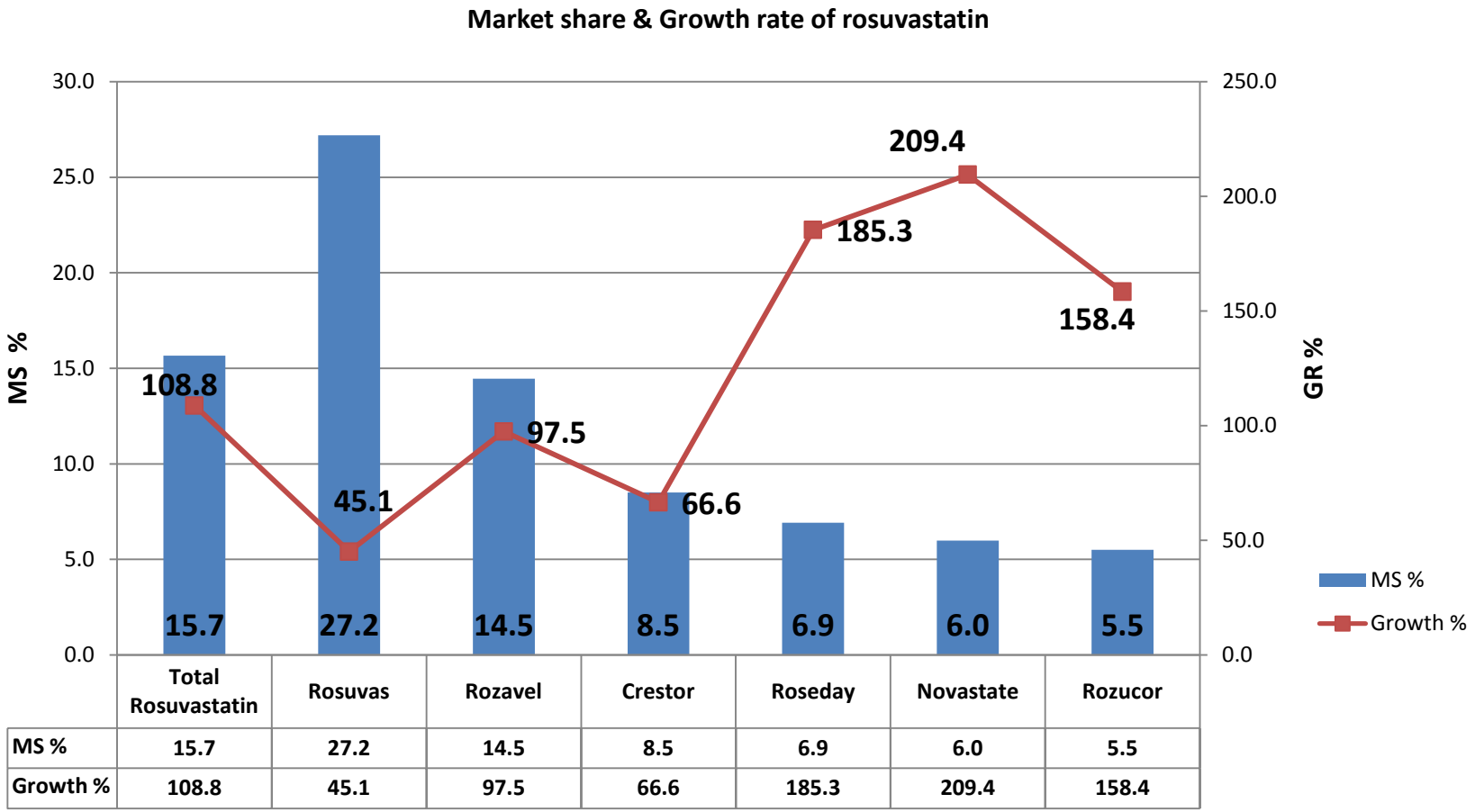


Storvas is the brand leader in atorvastatin therapy. **Modlip** sales in 2014 is 15.14 *crore* Rs.



	Atorvastatin	storvas	Aztor	Tonact	Atorva	Lipicure	Modlip
MS %	78.3	15.5	9.7	9.2	8.5	6.4	2.0
Growth %	8.7	7.0	12.5	9.1	8.0	21.9	-6.0

- Brand leader storvas is having market share of 15.68%.
- Modlip has a market share of 2.01 % however there is a slight degrowth of modlip about 6.01% in 2014.



	Total Rosuvastatin	Rosuvas	Rozavel	Crestor	Roseday	Novastate	Rozucor
MS %	15.7	27.2	14.5	8.5	6.9	6.0	5.5
Growth %	108.8	45.1	97.5	66.6	185.3	209.4	158.4

- Rosuvas growth rate is 45.13% which is less than the growth rate of Rozucor i.e 158.41%.

PRIMARY RESEARCH

& THEIR FINDINGS

Research Methodology

Research Plan

- Data source : Primary & secondary data
- Data type collected : Qualitative & Quantitative

Research Approach

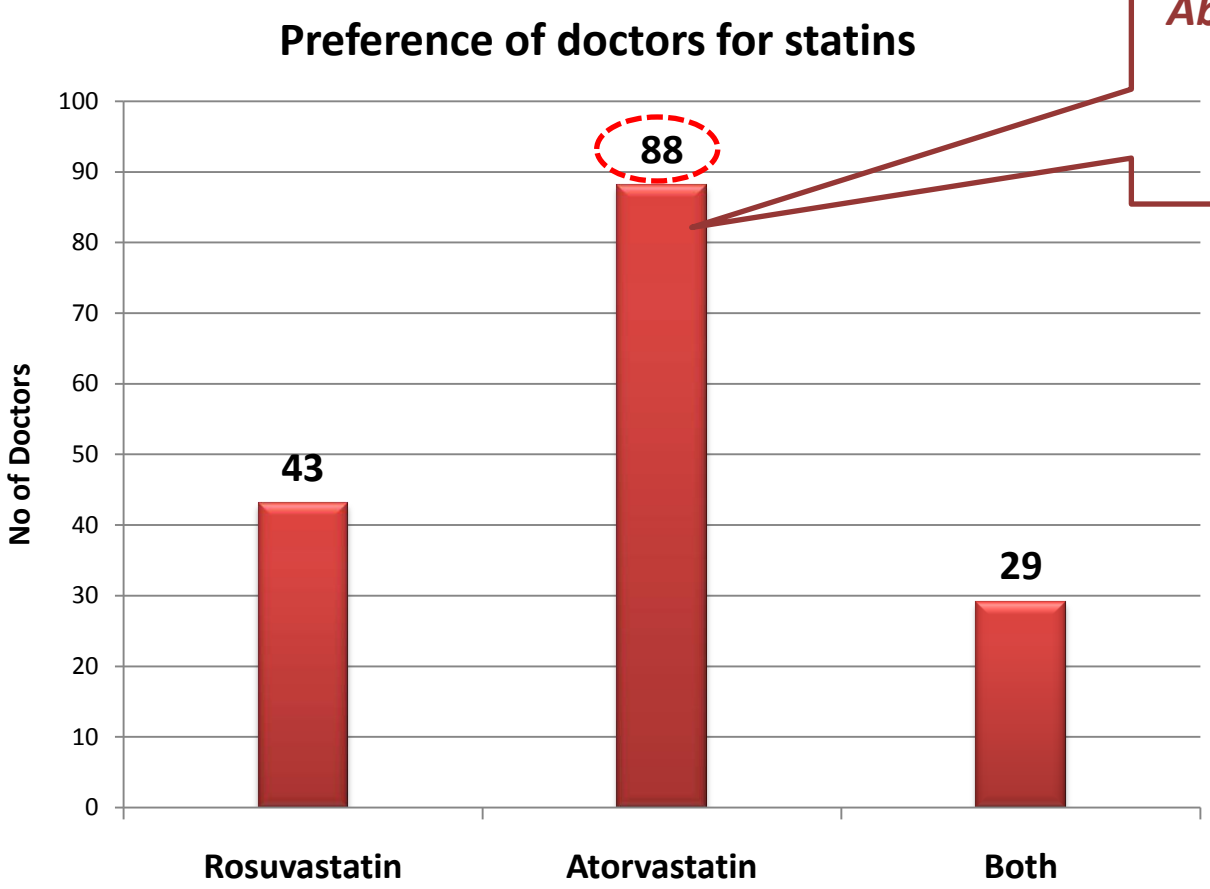
- City : Ahmedabad
- Respondents : CP's (156) , Cardiologist (4)
- Sample size(N) : 160

Research Tool

- Questionnaire
  - Open ended questions (2)
  - Close ended questions (9)

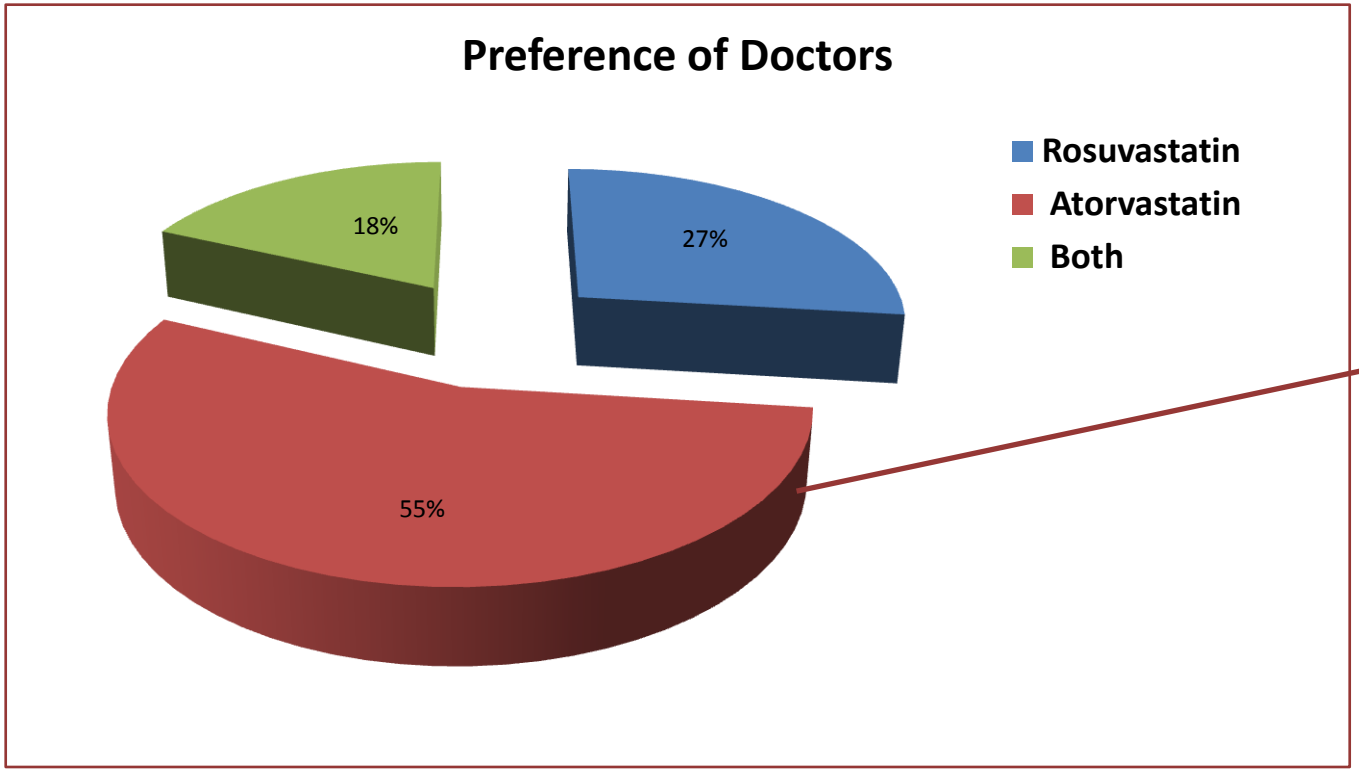
Preference of doctors as a First line therapy

Que-1. As a 1st line therapy which statin do you normally prefer?



About Half of the Doctors prefer Atorvastatin as a First line therapy of Hyperlipidemia.

N=160



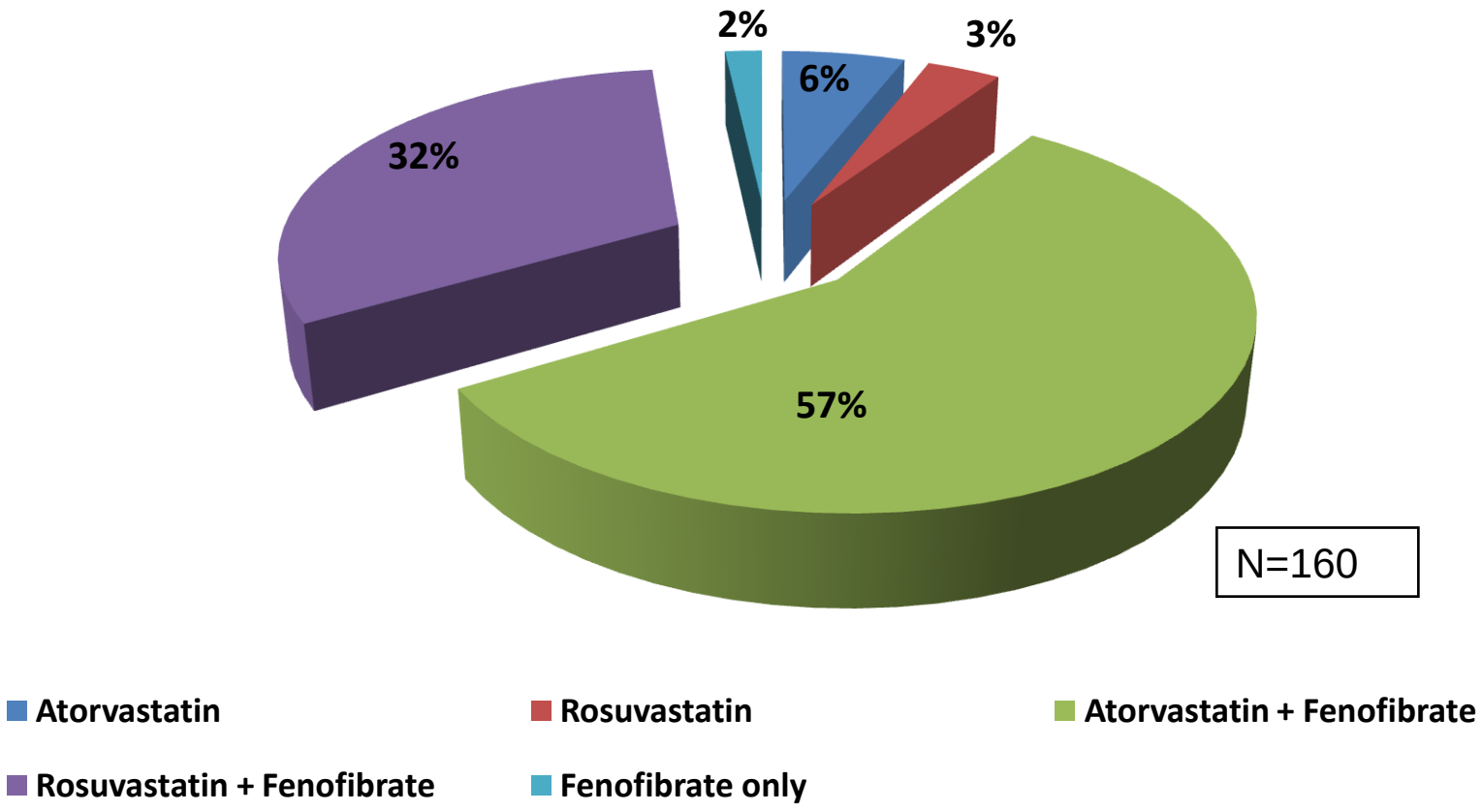
55 % of the doctors prefer Atorvastatin as a first line therapy of hyperlipidemia.

❑ INFERENCE

- Atorvastatin is well studied molecule and Recommended by NCEP guidelines so most of the Doctors prefer to prescribe Atorvastatin
- Rosuvastatin is a newer molecule compared to atorvastatin also less no of clinical data is available on the use of Rosuvastatin
- 18 % doctors use both atorvastatin and Rosuvastatin as a first line agent

Preference of Doctors in the treatment of Diabetic dyslipidaemia

Que-2. In diabetic dyslipidaemic patients, where increase in TG is of concern, which medication you prefer?



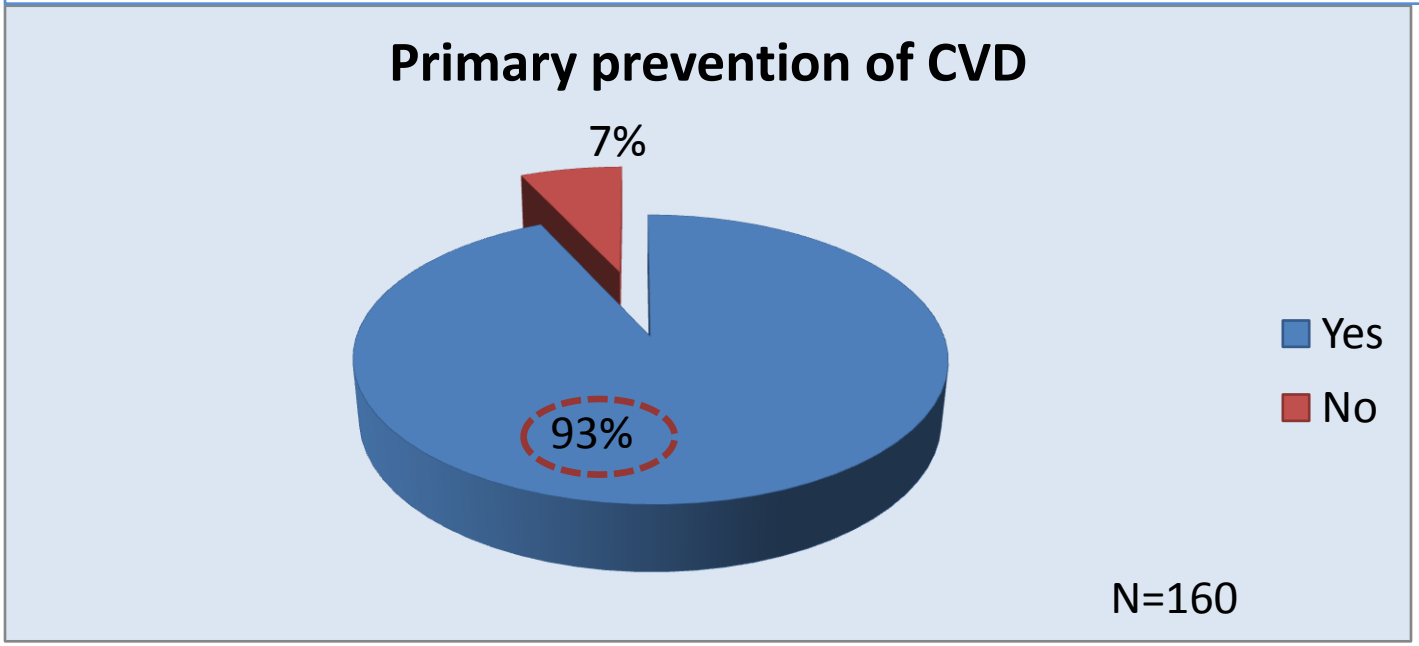
Inference

- 57 % Doctors prefer Atorvastatin + Fenofibrate & 32 % prefer Rosuvastatin + Fenofibrate combination for the treatment of Diabetic dyslipidaemic patients
- 2 % doctors use Only Fenofibrate for the treatment of diabetic dyslipidemia

- From the result we can conclude that Atorvastatin with the combination with Fenofibrate significantly reduce the TG level compared to the monotherapy.so it is the best treatment option available for diabetic dyslipidemia
- There are three reasons Doctors prefer Atorvastatin + Fenofibrate over Rosuvastatin + Fenofibrate
  - New to the market
  - Expensive
  - Less clinical data

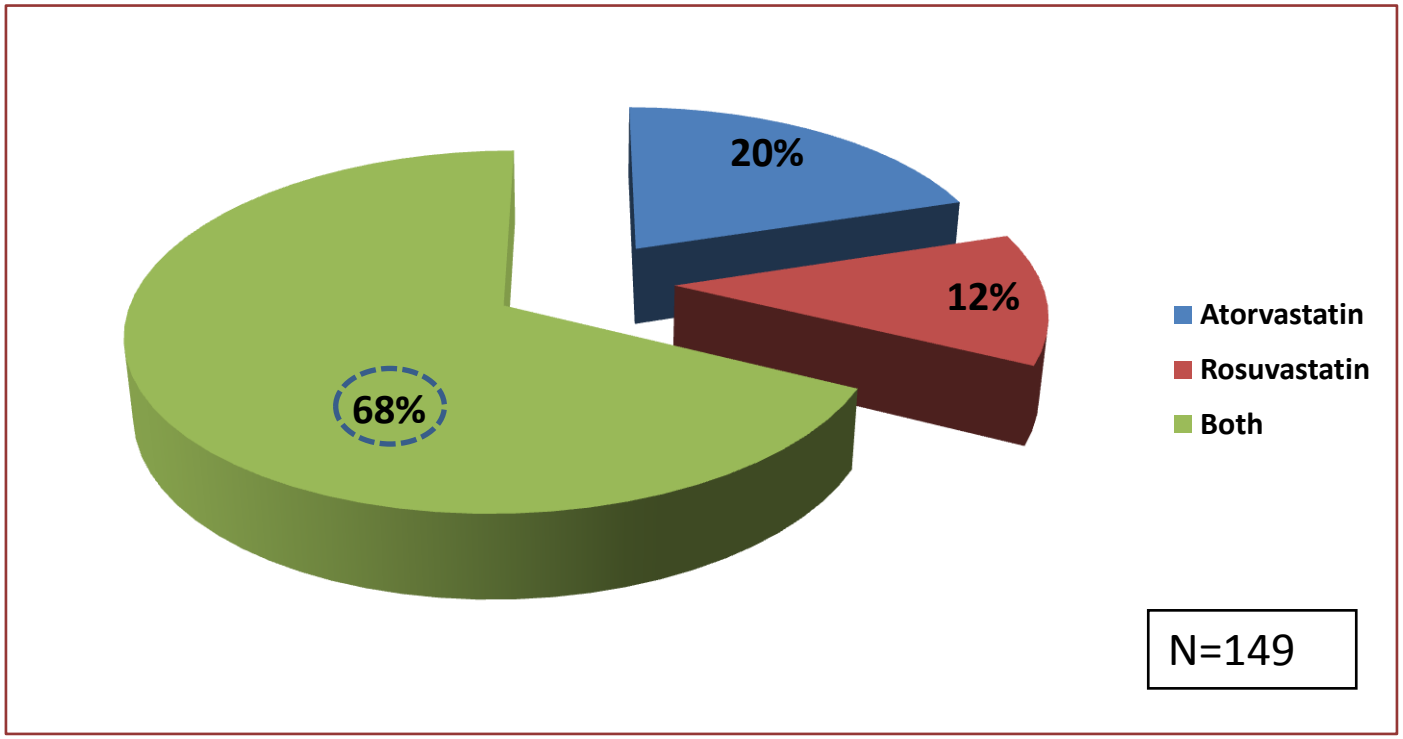
Choice for primary prevention of CVD

Que-3a. Do you prescribe statins for the primary prevention of CVD? (In patients with normal cholesterol but having risk factors)



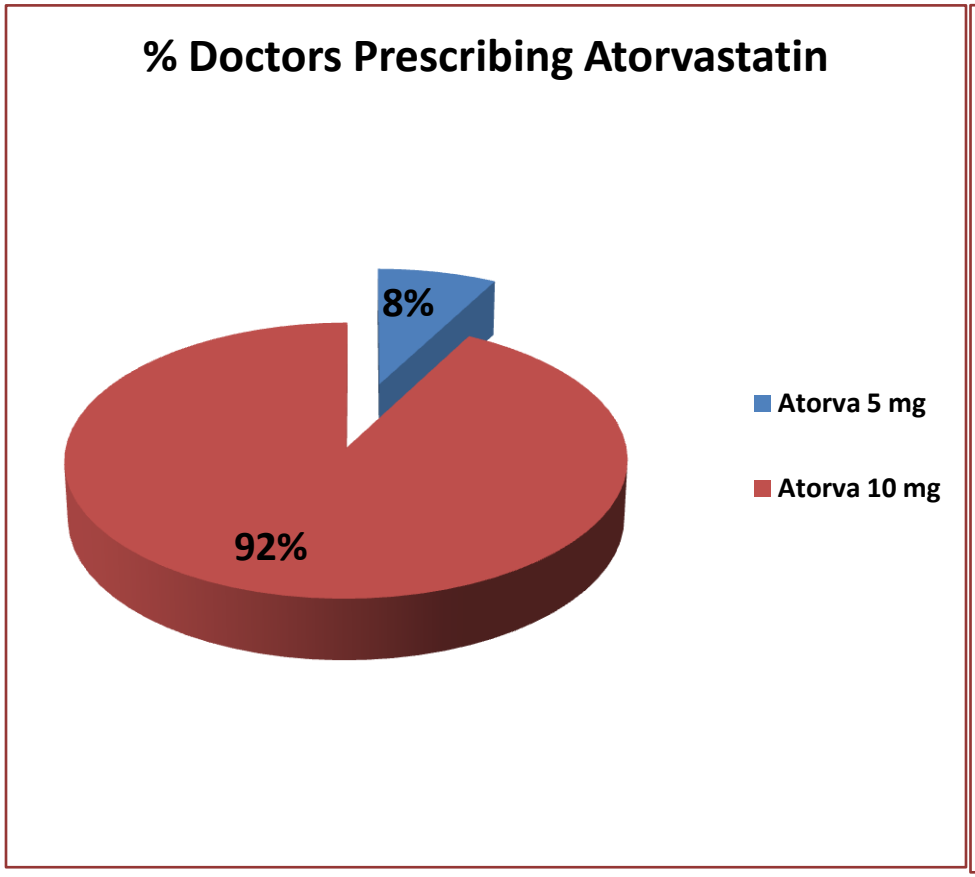
- This result shows that statins can be used in primary prevention of various Cardiovascular diseases. (i.e. ACS, Acute MI, Atherosclerosis)
- There is large opportunity for the atorvastatin molecule to be used in primary prevention of Acute MI, Atherosclerosis and other cardiovascular events

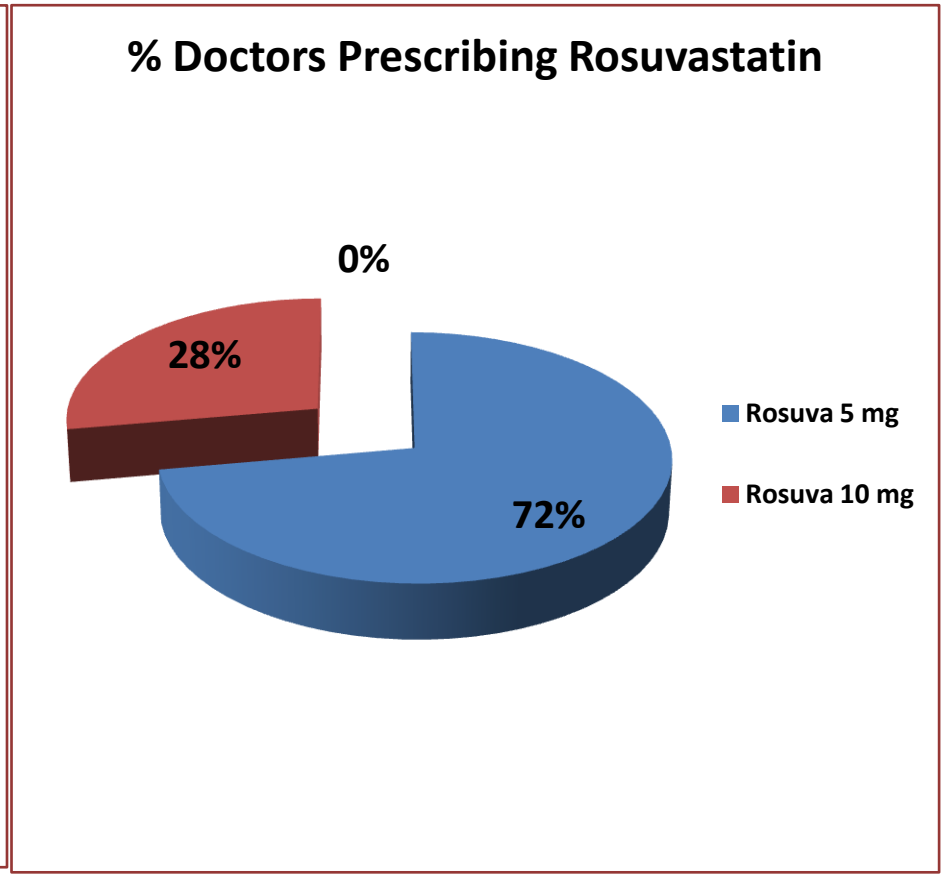
Que-3b. If Yes which statin do you prefer and which strength?



❑ **INFERENCE**

- Most of the Doctors prefer both Atorvastatin and Rosuvastatin for the primary prevention of CVD
- 20% and 12% doctors prefer only Atorvastatin and only Rosuvastatin respectively

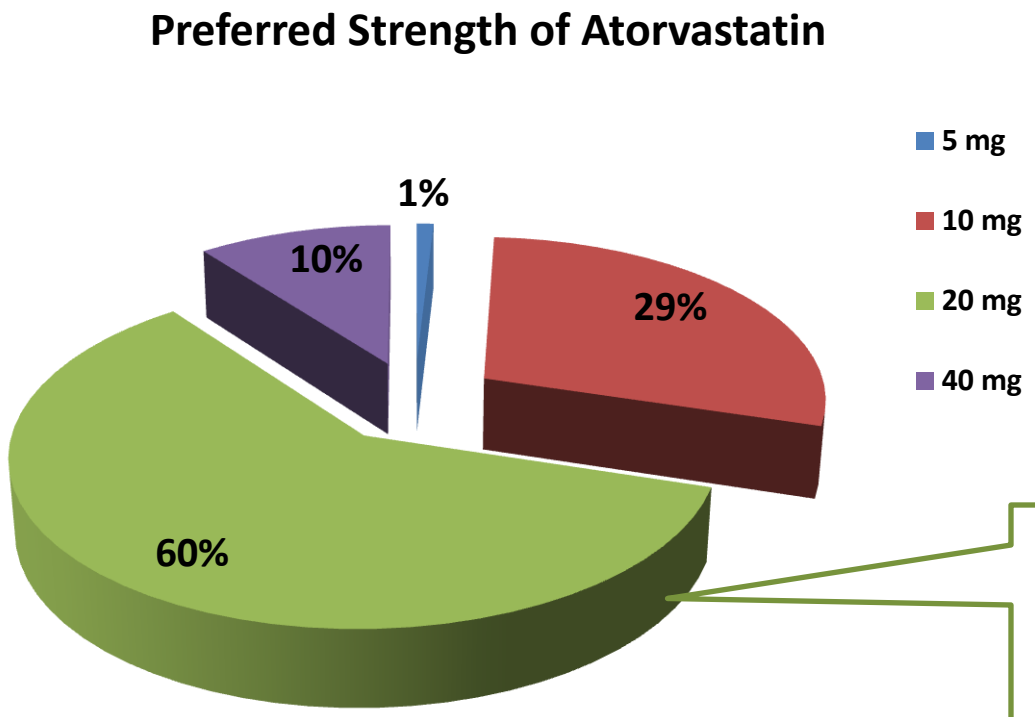




- Most of the Doctors prefer Atorvastatin 10 mg for the primary prevention of CVD
- Whereas 72 % doctors prefer Rosuvastatin 5 mg

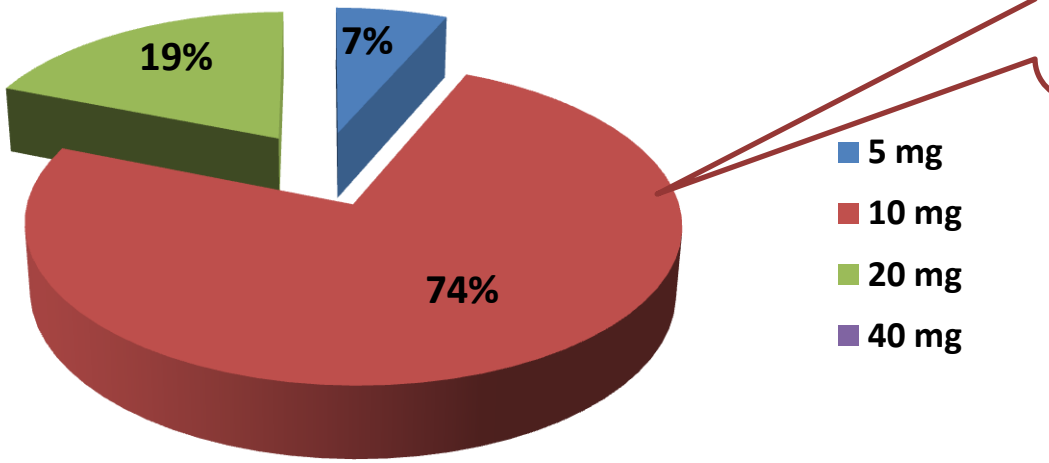
Most Prescribed Strength for achieving LDL-C goals

Que-4. With which strength of Atorvastatin or Rosuvastatin do you normally observe majority of patients achieving their LDL-C goals?



Atorvastatin 20 mg is mostly prescribed by the doctors to achieve LDL-C goals.

Preferred Strength of Rosuvastatin



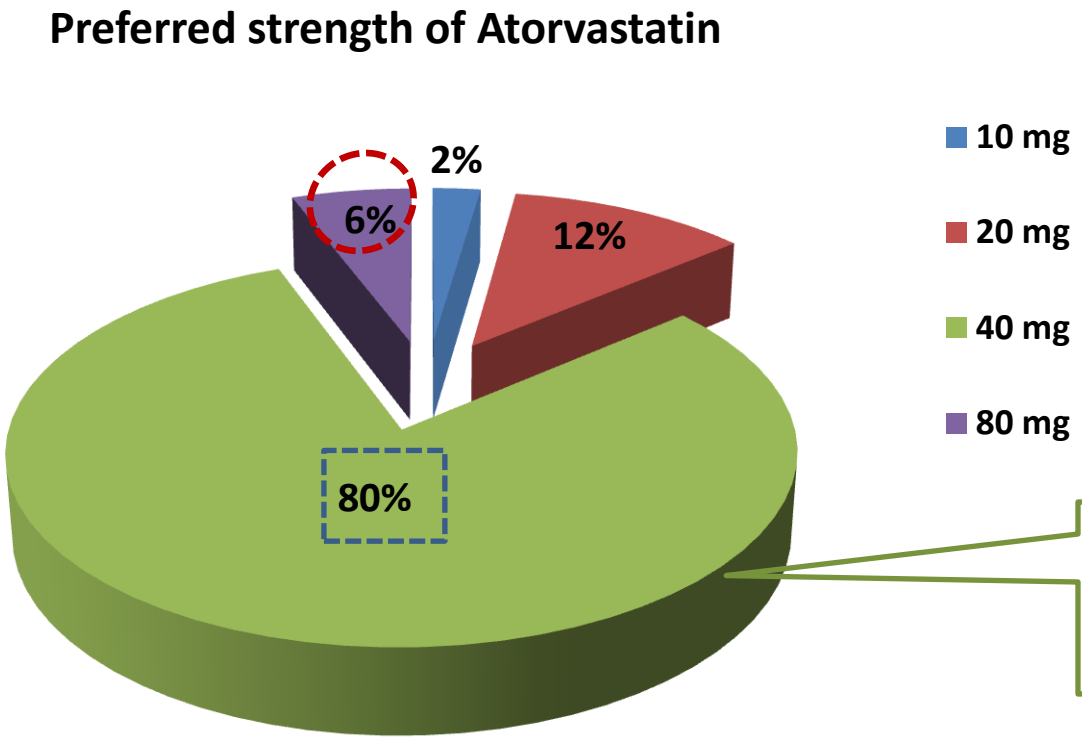
Rosuvastatin 10 mg is most prescribed for achieving the LDL-C goals.

❑ **INFERENCE**

- Most of the patients achieve their LDL-C goals with the strength of Atorvastatin 20 mg and Rosuvastatin 10 mg
- Most of the doctors said that usually strength is decided after checking the LDL-C levels. If the LDL-C level is slightly high they usually start the treatment with Atorvastatin 20 mg or Rosuvastatin 10 mg

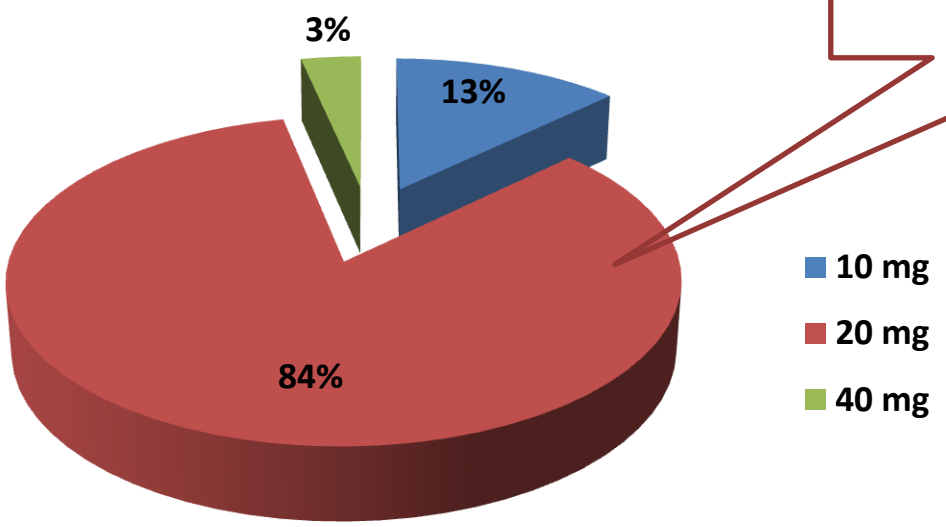
Preferred Strength for High Risk patients

Que-5. In high risk patients who require lower cholesterol goals (LDL-C< 70mg/dl) which strength of the following statin do you prefer?



80 % of doctors preferred atorvastatin 40 mg for high risk patients.

Preferred Strength of Rosuvastatin



84 % doctors prefer Rosuvastatin 20 mg for high risk patients.

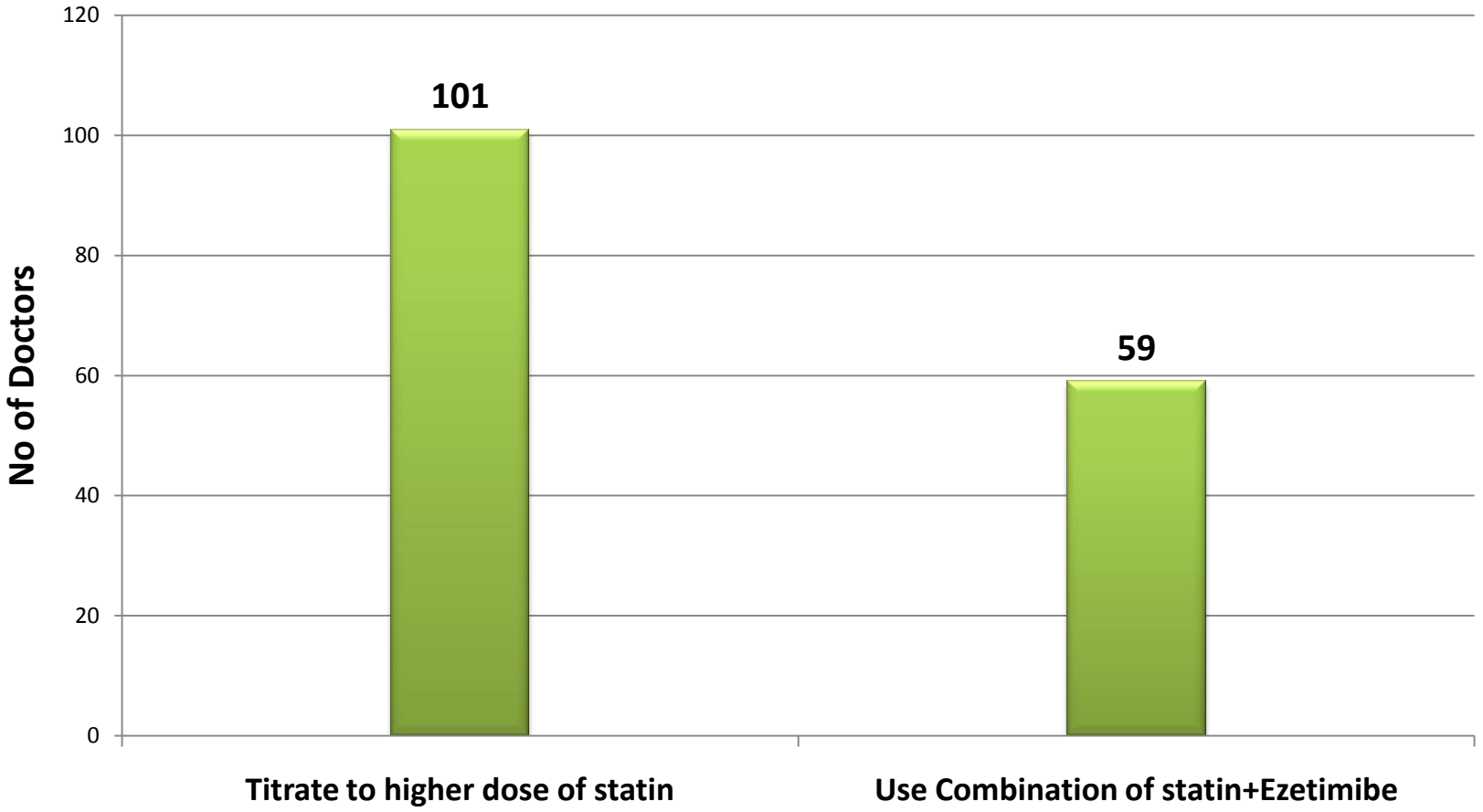
Rosuvastatin 40 mg is less preferred by doctors because less availability of safety and Efficacy data

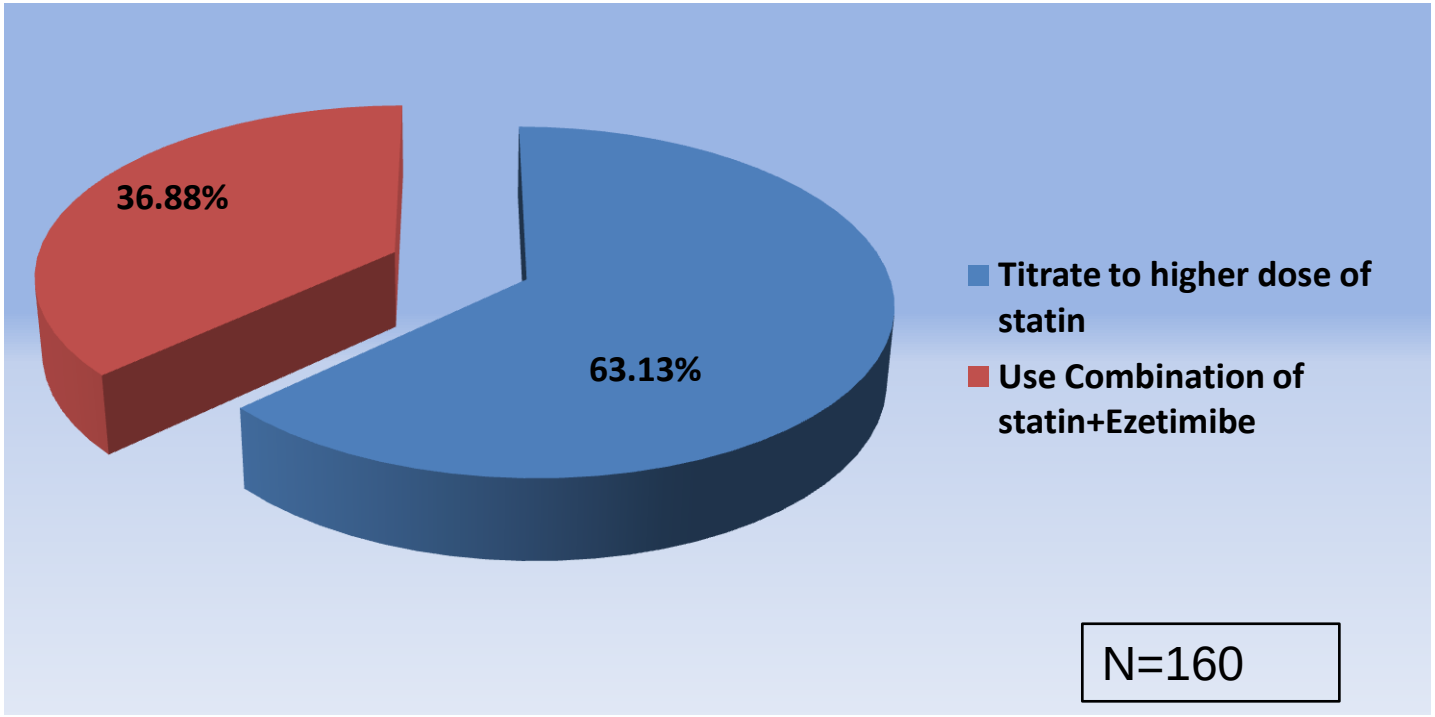
❑ INFERENCE

- Only 6% doctors prescribe atorvastatin 80 mg which shows that less no of CPs prescribe atorvastatin 80 mg
- CPs usually does not prescribe Atorvastatin 80 mg because of high risk of developing musculoskeletal side effects. They therefore prefer Atorvastatin 40 mg
- Mostly Cardiologist prescribe Atorvastatin 80 mg when there is a patient with high risk factors and with high LDL-C levels however they usually switch to lower doses after 10-15 days

Preference for combination with Ezetimibe

Que-6. **In patients at high risk do you titrate to higher doses of statin or prefer to use a combination with ezetimibe? (To attain LDL-C goals)**



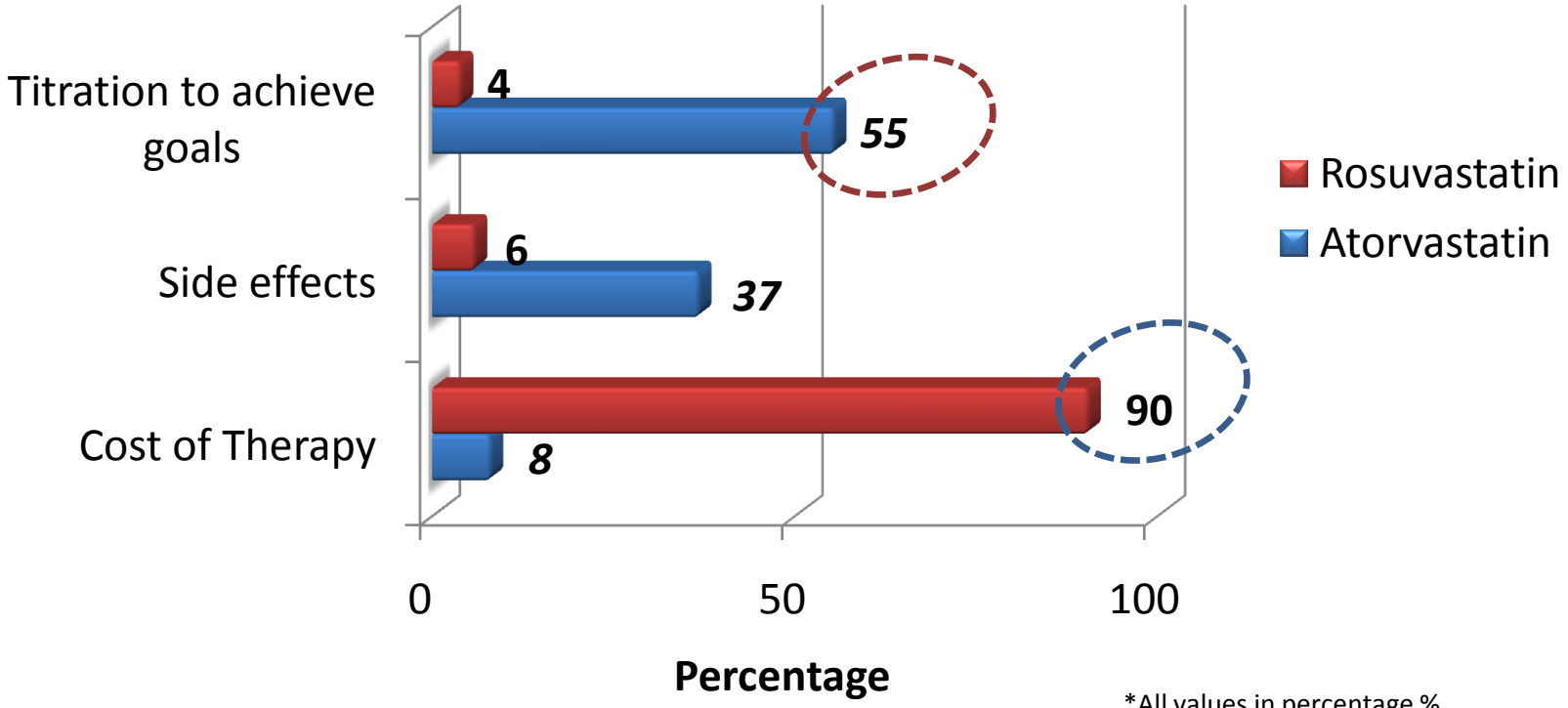


❑ INFERENCE

- 63.13 % doctors titrate to higher dose of statin to attain the LDL-C goals
- 36.88 % doctors use combination of statin + ezetimibe
- Less safety and pharmacokinetic data is available for the combination so doctors usually titrate to higher dose of statin rather to use combination

Factors affecting statin therapy

Que-7. What according to you are the major concerns in patients undergoing statin therapy?



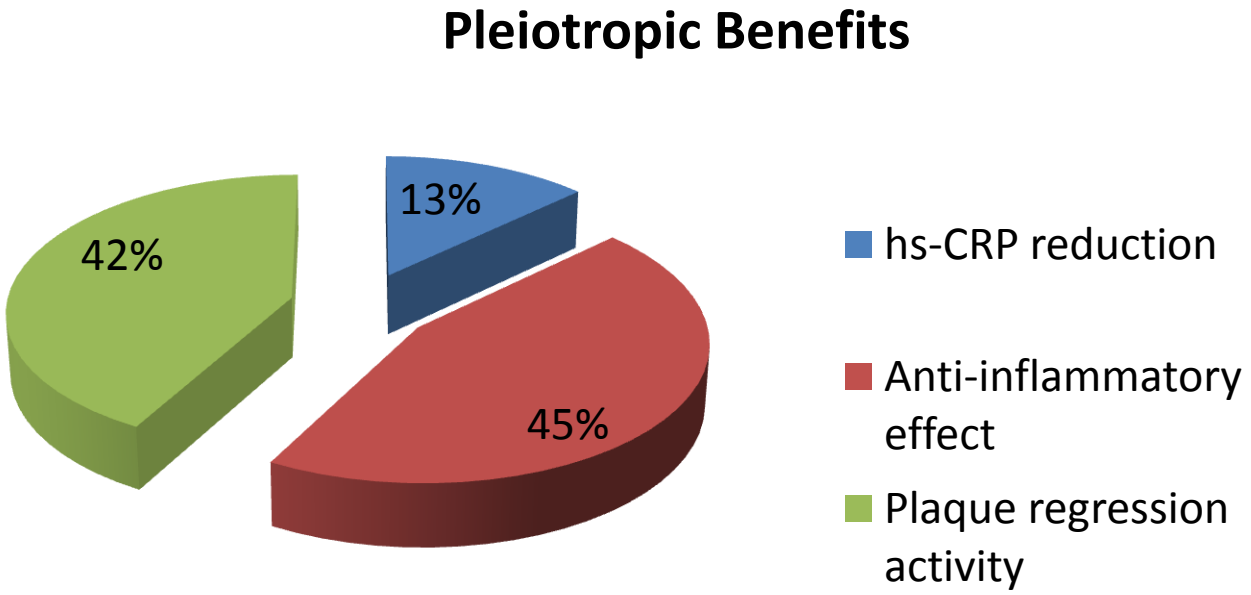
*All values in percentage %

❑ **INFERENCE**

- Rosuvastatin is a costly molecule so main limiting factor experienced by the doctors to prescribe Rosuvastatin widely is cost
- Atorvastatin is a cheap molecule compared to Rosuvastatin but titration is main concern to achieve the LDL-C goals

Comparison based on Pleiotropic benefits

Que-8. According to you, which pleiotropic benefits of Atorvastatin scores over Rosuvastatin?



❑ **INFERENCE**

➢ Most of the doctors said that pleiotropic benefits i.e. Anti-inflammatory effect and plaque regression activity of atorvastatin is good compared to rosuvastatin

Perception of Doctors

Que-9. **Please (✓) your opinion on following statements. [1=Strongly Disagree, 5= strongly agree]**

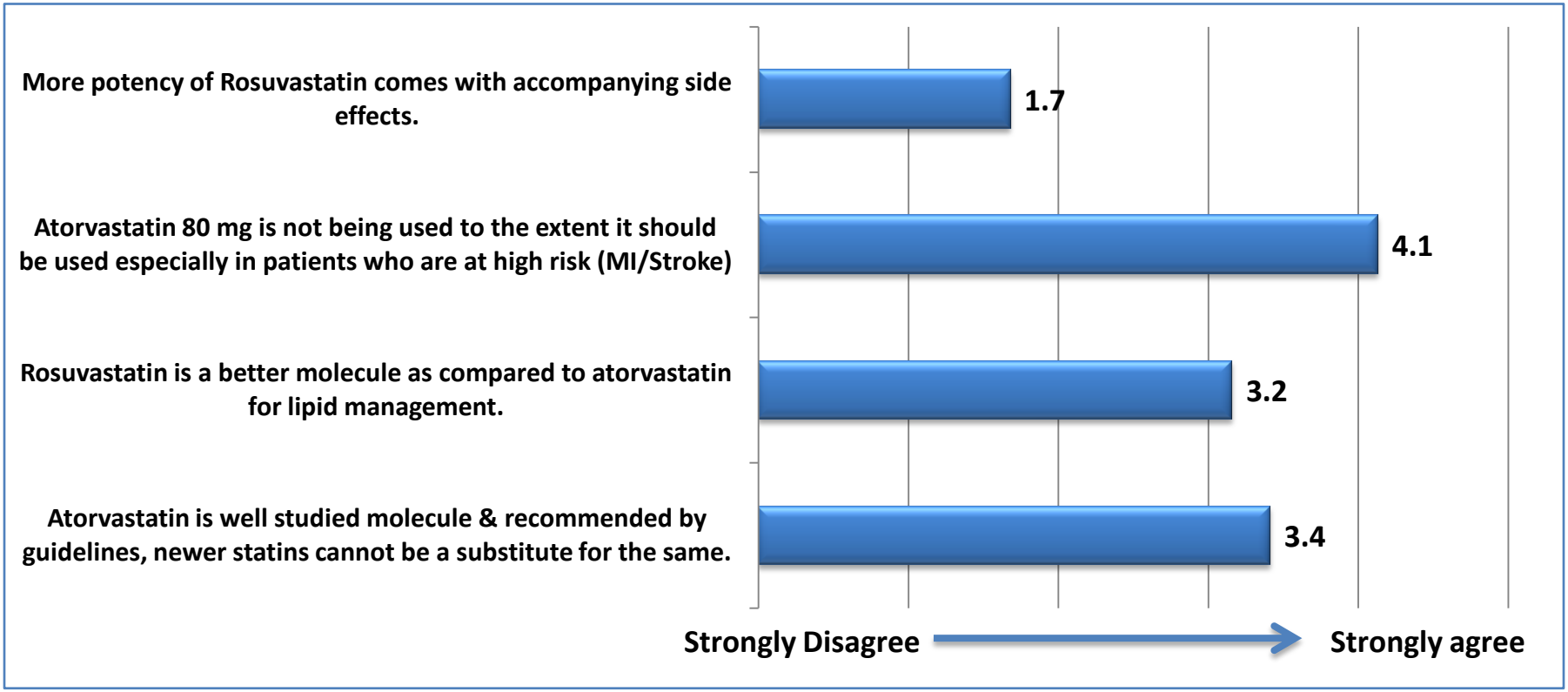
(a) Atorvastatin is well studied molecule & recommended by guidelines, newer statins cannot be a substitute for the same.

(b) Rosuvastatin is a better molecule as compared to atorvastatin for lipid management.

(c) Atorvastatin 80 mg is not being used to the extent it should be used especially in patients who are at high risk (MI/Stroke)

(d) More potency of Rosuvastatin comes with accompanying side effects.

Statements	Strongly Disagree	Disagree	Somewhat Agree	Agree	Strongly agree
Atorvastatin is well studied molecule & recommended by guidelines, newer statins cannot be a substitute for the same.	5.0%	11.9%	33.1%	36.9%	13.1%
Rosuvastatin is a better molecule as compared to atorvastatin for lipid management.	3.8%	25.0%	35.6%	24.4%	11.3%
Atorvastatin 80 mg is not being used to the extent it should be used especially in patients who are at high risk (MI/Stroke)	5.0%	2.5%	9.4%	40.6%	42.5%
More potency of Rosuvastatin comes with accompanying side effects.	49.4%	38.1%	8.1%	4.4%	0.0%

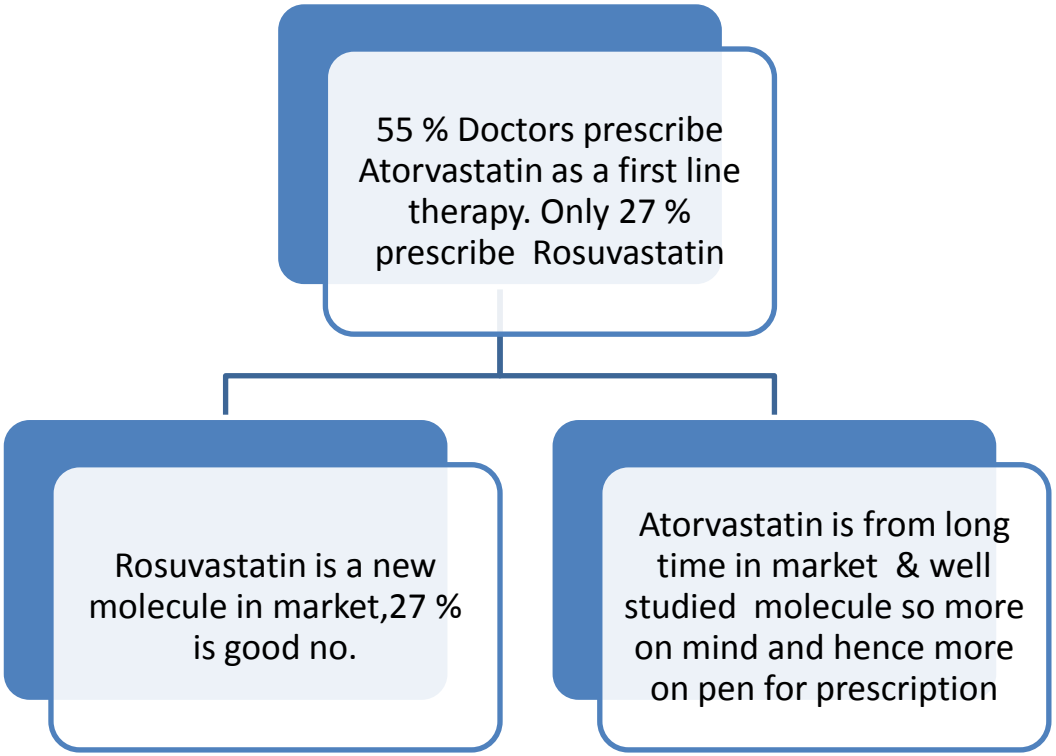


❑ INFERENCE

- Most of the Doctors are Somewhat agree to the statement that Atorvastatin is a well studied molecule and newer statin can not be the substitute for the same
- Doctors are strongly agreed to the statement that Atorvastatin 80 mg is not being used to the extent it should be used in a patients who are at high risk
- There is a neutral response for the statement that Rosuvastatin is a better molecule for lipid management

Key Findings

- Atorvastatin is leading molecule in current Statins market with highest market share.
- 55 % doctors prescribe atorvastatin and 27 % doctors prescribe rosuvastatin. Rosuvastatin is a new molecule however its usage is increasing very fast



Cont...

- Most of the doctors prefer atorvastatin+ Fenofibrate combination(57%) to lower the TG level in a diabetic dyslipidaemic patients and Less no of doctors use plain fenofibrate in diabetic dyslipidaemic patients
- Majority of the Doctors prescribe Atorvastatin 10 mg (92%) and Rosuvastatin 5 mg (72%) for the primary prevention of CVD. This shows that Rosuvastatin is a potent molecule compared to atorvastatin
- CP's usually prefer Atorvastatin 40 mg or Rosuvastatin 20 mg for High risk patients
- 90 % of doctors said that they do not prescribe Rosuvastatin because it's a costly molecule so every patient can not afford it. So cost of therapy is of main concern while prescribing Rosuvastatin

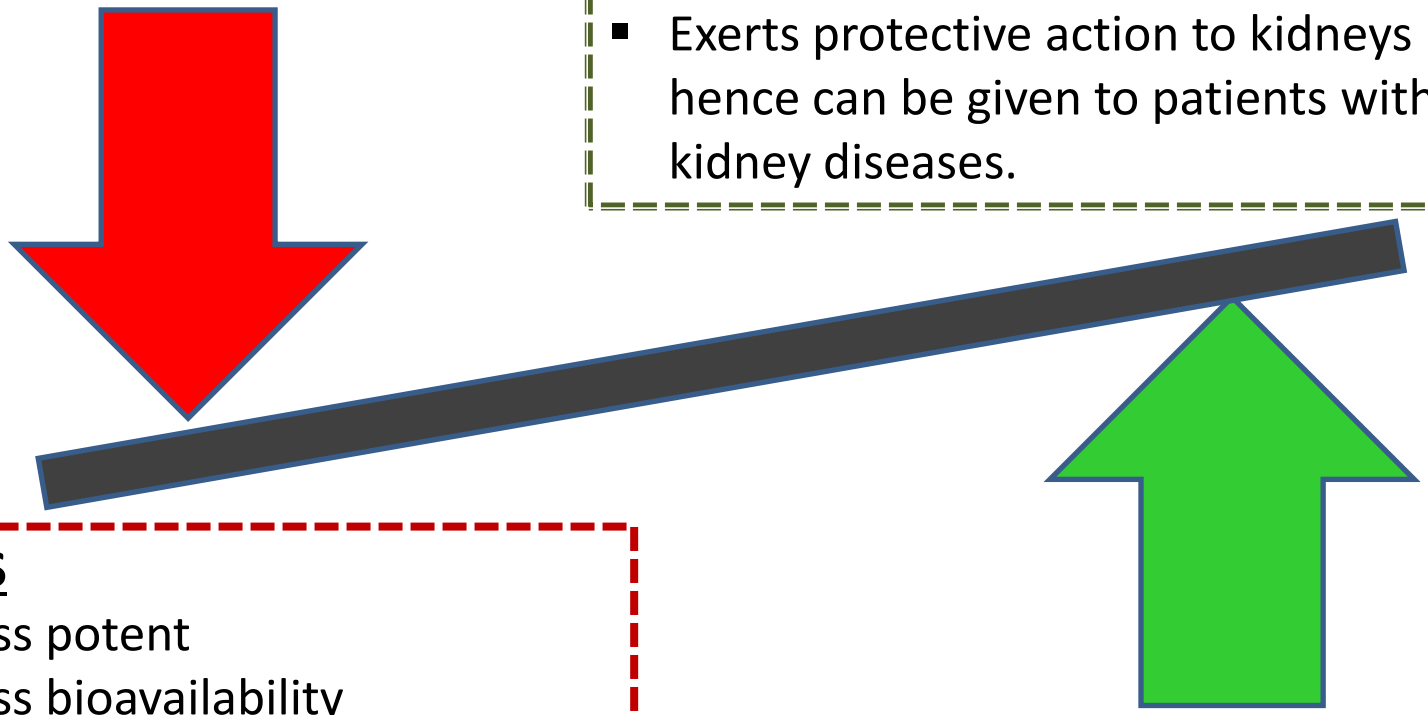
Cont...

- Majority of the patients agreed to the statements that Atorvastatin is a well studied molecule and any newer statin cannot be the substitute for the same
- Most of the doctors agreed to the statement that atorvastatin 80 mg is not being used to the extent it should be used in high risk patients
- Although Rosuvastatin is a potent molecule but it doesn’t have a more side effects

Atorvastatin Molecule

PROS

- Well established and old Molecule
- More clinical data is available
- Less costly
- Exerts protective action to kidneys hence can be given to patients with kidney diseases.



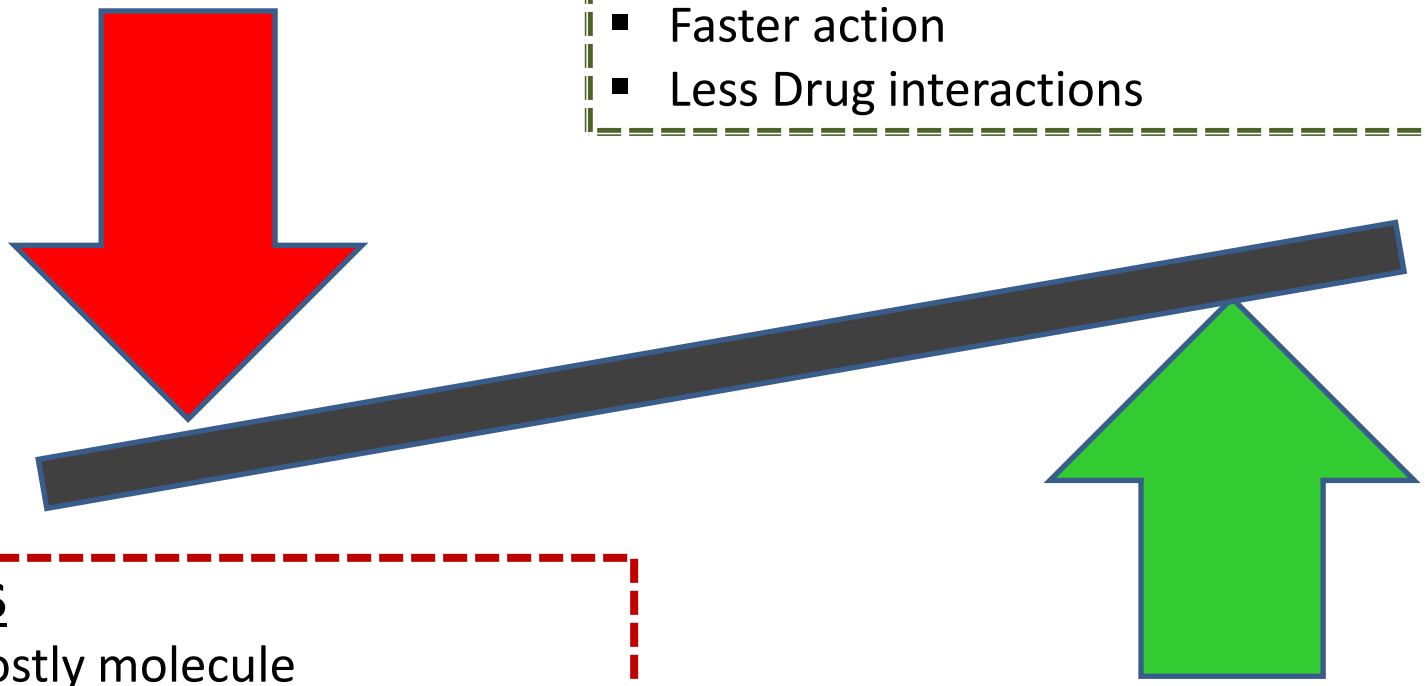
CONS

- Less potent
- Less bioavailability

Rosuvastatin Molecule

PROS

- Higher potency
- Faster action
- Less Drug interactions



CONS

- Costly molecule
- Can't be given to the patient with impaired kidney function

Suggestions

- Since Atorvastatin is the leading molecule with the highest market share in the current statin market newly launched Rosuvastatin molecule is gaining acceptance in the market which will be a greater threat to atorvastatin market in India
- Create the awareness about the advantages of atorvastatin among the doctors.
- The campaign should be chiefly targeted to **KOL's** in the field of **Cardiology, Diabetology** and then should be gradually extended to remaining **Consulting cardiologist** and physicians
- Doctors should be made aware of the fact that atorvastatin is a widely studied molecule with more than 400 clinical studies

Cont...

- Atorvastatin + Fenofibrate combination should be strongly promoted to the doctors those uses **only Fenofibrate** in the treatment of Diabetic dyslipidaemic patients
- Promotion should be based on cost because atorvastatin + fenofibrate combination is less costly compared to Rosuvastatin + fenofibrate combination
- Try to increase the usages of atorvastatin 10 mg for the primary prevention of CVD by providing sufficient clinical evidence to the doctors
- **Build up the confidence** into the mindset of Consulting physicians and cardiologists to prescribe higher strength of atorvastatin (i.e. **Atorvastatin 80mg**) by providing sufficient clinical evidences

Cont...

- Atorvastatin is mostly prescribed due to its lower cost if in future cost of rosuvastatin molecule decreases that will create major threat to atorvastatin molecule so to remain in the competition try to cut down the cost
- Statin combination therapy will be a better option in the future. So focus more on the combination therapy

THANK YOU