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| **PROTOCOL TITLE:** The use of hepatitis C donor organs in hepatitis C negative recipients | |
| **APPLICABLE FACILITIES:**  EHC EDH EHH EHI EHN EJCH ELTAC ESJH  EUH EUHM EUHS EUOSH EWWH RJV-ERH RJV-ESOP TEC/ESA | |
| **EFFECTIVE DATE:** | **ORIGINATION DATE:** |

**CATEGORY:**

Choose One or More: **Diagnostic/Therapeutic/Preventive**, **Medication Guidelines**  **Teaching**

**LEVEL:**

Choose One: Dependent, **Independent**, or Interdependent

**CONTENT:**

**Protocol**

1. This protocol applies to potential transplant recipients that are Hepatitis C (HCV) negative that receive a donor organ from a HCV NAT seropositive donor.
2. Recipients who receive an organ from an HCV seropositive, but HCV NAT negative recipient will not automatically receive Direct Acting Antiviral (DAA) therapy. They will have an HCV viral load checked on POD7 and POD14 and then receive routine PHS increased risk surveillance labs (1 month, 3 months and 12 months post-transplant). If they are found to have contracted HCV by these surveillance labs, DAA therapy will be initiated at that time.
3. Prior to transplant, the recipient will be consented to receive a transplant organ that is positive for HCV.
4. Confirm Hepatitis B status by testing for HBV surface antigen (HBsAg), HBV surface antibody (HBsAb), and HBV core antibody (HBcAb).
   1. If found to be HBV positive, follow organ specific Hepatitis B protocol(s).
5. Prescription medication insurance must be verified and documented prior to transplant by the transplant coordinator or transplant finance team. Charity care transplant recipients are ineligible to receive a donor organ from a HCV positive donor.
6. Intra-operative donor biopsies will be obtained during organ procurement for all livers taken from HCV positive donors for use in HCV negative recipients. If possible, the HCV viral load of the donor will be obtained.
7. HCV positive donors who are of more advanced age or who are co-infected with HBV (HCV+ HBcAb+ donors) will be considered for this protocol per surgeon discretion.
8. Recipients listed for multiple organ transplants (e.g. simultaneous liver-kidney or simultaneous heart-kidney transplant candidates) will be eligible to receive organs under this protocol.
9. On POD #1:
   1. The transplant recipient will have a HCV viral load and genotype collected.
      1. The HCV PCR is run on Monday/Wednesday/Friday if specimen received by 05:00.
   2. Initiate inpatient hepatology consult.
10. On POD #1-7:
    1. The transplant recipient will start DAA therapy with either Epclusa (sofosbuvir 400mg/velpatasvir 100mg) taken once daily for 8 weeks or Mavyret (glecaprevir 100mg/pibrentasvir 40mg) take 3 tablets po daily for 8 weeks. Therapy duration can be extended beyond 8 weeks at the discretion of the team.
       1. Epclusa (sofosbuvir 400mg/velpatasvir 100mg) will be the preferred agent except for transplant recipients on hemodialysis or with severe renal impairment (eGFR <30ml/min) at the time of therapy initiation. Mavyret (glecaprevir 100mg/pibrentasvir 40mg) will be the preferred agent for patients with severe renal impairment.
    2. HCV viral load will be obtain on POD3, POD5, and POD7.
       1. The HCV PCR is run on Monday/Wednesday/Friday if specimen received by 05:00.
    3. The Provider sends an EEMR message via PowerChart to The Center for Viral Hepatitis.
       1. The Center for Viral Hepatitis sends an outlook notice to the schedulers to create an EUHM encounter
       2. EUHM encounter is created within 24-48 hours of request
       3. Medication (DAA) is to be ordered from the EUHM encounter by the clinical team at The Center for Viral Hepatitis.
       4. The outpatient hepatitis pharmacist will review the HCV medication received from The Pharmacy at Emory. The hepatitis pharmacy team may assist with any insurance authorizations or prior authorizations needed.
11. Laboratory Monitoring
    1. HCV viral load (PCR) at weeks 2, 4, 8, and 12
       1. The HCV PCR is run on Monday/Wednesday/Friday if specimen received by 05:00.
    2. Sustained Virologic Response (SVR): SVR 2, SVR 4, SVR 12, SVR 24
    3. Other labs per transplant team
    4. Labs per PHS high risk protocol (1 month, 3 months and 12 months)
12. Prior to discharge, no later than the day of discharge
    1. The Center for Viral Hepatitis review of patient information with confirmation of appointment
       1. Appointment day and time should be given to the patient prior to discharge
    2. The patient receives Epclusa (sofosbuvir 400mg/velpatasvir 100mg) or Mavyret (glecaprevir 100mg/pibrentasvir 40mg) for outpatient use from the Pharmacy at Emory (28 tablets if sofosbuvir/velpatasvir, 84 tablets if glecaprevir/pibrentasvir). Another pharmacy may be utilized if the patient’s insurance requires it.
    3. The patient received an updated medication list and education on the HCV medication(s) in addition to transplant medications
13. Patient follow up for HCV
    1. The patient is to be seen by the Center for Viral Hepatitis starting at 4 weeks post-transplant and every 4 weeks thereafter for a total of 5 months or a time at the providers discretion
14. Medication Considerations
    1. **Epclusa** (sofosbuvir 400mg/velpatasvir 100mg)
       1. Genotypes: 1-6
       2. **Dose**: Sofosbuvir 400mg and velpatasvir 100mg po qday
       3. **Duration**: 8 – 12 weeks of treatment
       4. **Use in renal insufficiency**: Sofosbuvir metabolite may accumulate if eGFR is <30ml/min. Consider using Mavyret (glecaprevir 100mg/pibrentasvir 40mg) if several renal insufficiency and is expected to be chronic.
       5. **Food**: May be taken with or without food
       6. **Common adverse effects**: headache, fatigue, insomnia, nausea, diarrhea
       7. **Drug Interactions:**
          1. Amiodarone – Concomitant use may cause severe bradycardia. Recommend cardiac monitoring while inpatient. Upon discharge, patient should be instructed to monitor BP/HR at least 1 time per week or as otherwise instructed by the transplant team.
          2. Acid reducing medications:
             1. May decrease the effectiveness of Epclusa (sofosbuvir/velpatasvir)

1st choice: No acid reducing medications

2nd choice: Famotidine 20mg once daily or q12hr.

H2 blockers should be taken at the same time as Epclusa (sof/velpatasvir) or 12 hours apart.

3rd choice: Antacids (Maalox, Mylanta, Tums, etc) should be avoided or separated from Epclusa by at least 4 hours.

4th choice: Proton Pump Inhibitors (PPIs) ideally should be avoided. If they cannot be avoided, patients should take no more than 20mg of omeprazole equivalent 4 hours after taking Epclusa (sof/velpatasvir) with food.

* + - 1. Statins – Can increase the levels of rosuvastatin, atorvastatin and likely simvastatin which can increase the risk of myopathy. It is recommended not to exceed 10mg of rosuvastatin daily. Avoid simvastatin and lovastatin in transplant recipients. Monitor for myopathy.
         1. Heart transplant patients may receive pravastatin 20mg po qhs per heart transplant protocol.
      2. Other potential drug interactions – consult pharmacist
  1. **Mavyret** (glecaprevir 100mg/pibrentasvir 40mg)
     1. **Genotypes**: 1-6
     2. **Dose**: Glecaprevir 100mg and pibrentasvir 40mg; 3 tablets daily
     3. **Duration**: 8 weeks of treatment
     4. **Use in renal insufficiency**: No renal dose adjustments necessary. Preferred agent in patients with severe renal insufficiency (eGFR <30ml/min) or in those patients requiring HD
     5. **Food**: Take with food
     6. **Common adverse effects**: Headache, fatigue, nausea, diarrhea
     7. **Drug interactions**: Many potential
        1. Statins – Mavyret (glecaprevir/pibrentasvir) can increase the levels of statins leading to an increased risk of myopathy. Recommend avoiding simvastatin, lovastatin and atorvastatin. Recommend not to exceed 10mg of rosuvastatin daily. Recommend 50% of the dose of pravastatin.
           1. Use pravastatin 10mg (reduced dose) po qhs in heart transplant recipients.
        2. Calcineurin Inhibitors (CNIs) – Mavyret (glecaprevir/pibrentasvir) may increase the levels of tacrolimus and cyclosporine. Use with caution. Monitor closely.
        3. Mammalian Target of Rapamycin Inhibitors (mTORi) – Mavyret (glecaprevir/pibrentasvir) may increase the levels of sirolimus and everolimus. Use with caution. Monitor closely.

**RELATED POLICIES / PROCEDURES**: Hepatitis C protocol, Hepatitis B protocol

**DEFINITIONS:**

**REFERENCES AND SOURCES OF EVIDENCE:**

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**KEY WORDS:** Hepatitis C, transplant, HCV NAT positive