Heart Transplantation From Hepatitis C–Positive Donors in the Era of Direct Acting Antiviral Therapy: A Comprehensive Literature Review

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**Background.** While heart transplantation is a highly effective treatment in patients with advanced heart failure, the number of people waiting for a transplant exceeds the number of available donors. With the advent of direct acting antivirals (DAA) for the eradication of Hepatitis C, the heart transplant donor pool has been expanded to include donors with untreated Hepatitis C. To help with the development of future protocols for Hepatitis C–positive heart transplants, we performed a review of the literature on DAA therapy in the context of heart transplantation. **Methods.** We searched MEDLINE, EMBASE, OVIDE JOURNAL, and GOOGLE SCHOLAR for papers published between 01.01.2011 and 01.06.2019 using key words “heart transplantation” associated with “hepatitis C.” **Results.** After removing duplicates, we screened 78 articles and retained 16 for primary analysis and 20 for sustained virologic response 12 weeks after completion of the DAA therapy (SVR-12). The data from 62 patients were extracted from these publications. Fifty-six (90%) patients had donor-derived hepatitis C and 6 (10%) patients were chronically infected with hepatitis C before transplantation. All living transplanted patients achieved SVR-12, defined as hepatitis C virus RNA below the limit of detection 12 weeks after treatment completion. Treatment duration ranged from 4 to 24 weeks. Clinically relevant modification to the dosing of immunosuppressive medications during DAA therapy was documented in only 1 patient (1.6%). Six (14%) patients experienced rejection during DAA therapy. **Conclusions.** Despite different timings of initiation of DAA therapy across the included studies, there were no differences in sustained viral clearance. Early commencement of DAA with a potentially shorter treatment duration (<8 wk) is appealing; however, further studies are required before recommending this approach.

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While heart transplantation is a highly effective treatment in patients with advanced heart failure, the number of people waiting for a transplant exceeds the number of available donors. In the United States alone, up to 350 people die each year awaiting heart transplant,1 and it has been estimated that if the donor pool was widened to include those with hepatitis C, >140 extra heart transplants could be performed annually.2 Hepatitis C virus (HCV) is an enveloped flavivirus with a parenteral mode of transmission.3 There are 6 viral genotypes with >67 subtypes.4 Before 2001, screening for hepatitis C in donors and recipients was not routinely performed. This led to numerous donor-derived hepatitis C (DDHC) infections5 and increased morbidity and mortality.6,7 As a result, donors with HCV were routinely excluded.

With the arrival of highly-effective direct acting antiviral (DAA) therapy including pan-genotypic DAA, transplantation of hepatitis C–positive donor organs,8-10 including hearts,11 has become a viable option. A growing number of protocols addressing this topic are being established and a number of centers are currently following patients who have received organs from HCV-positive donors.12-16 The most recent International Society of Heart and Lung Transplantation (ISHLT) conference abstracts include the largest published cohorts of transplant recipients undergoing successful

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Hepatitis C treatment\textsuperscript{5,17-26}; however, these studies are still on-going.

As expressed in the editorial by Givertz et al,\textsuperscript{27} transplantation of hearts from hepatitis C–positive donors (either RNA and/or antibody positive) has presented clinicians with an opportunity to expand the donor pool and close waitlist gaps. It is also an opportunity for marginal recipients to significantly shorten the waiting list times by accepting a heart from a hepatitis C–positive donor. In 1 center, the mean waitlist time was 329 days for those receiving an HCV negative graft and 78 days in those accepting a Hepatitis C–positive graft.\textsuperscript{28} In another cohort, the waitlist time for Hepatitis C–positive grafts was as little as 4 days.\textsuperscript{5} However, some questions remain unanswered that need to be addressed before heart transplantation from HCV-positive donors becomes the standard of care.

The objective of our review was to analyze the currently published literature to address the following questions: what is the efficacy of DAA in the setting of heart transplantation? What interactions between immunosuppression and DAA have been documented? Does DAA increase the risk of acute rejection? What is the optimal timing for the initiation of DAA? And what is the most favorable duration of therapy?

**MATERIALS AND METHODS**

**Search Method**

We utilized PRISMA flow-chart to plan our review.\textsuperscript{29} An electronic search was performed in Medline, Embase, Ovide journal, and Google Scholar to identify all articles and abstracts in English, French, and German published between 01.01.2011 and 01.06.2019. We chose this particular time frame to cover the era of direct DAA therapy.

In order to set up the search, we used keywords, automatic generated synonyms (in Ovid), and MESH terms. We searched for “heart transplantation” associated with “hepatitis C” or with “direct-acting antiviral” in the title of the publication. In an attempt to cover all the available literature, we use 3 predefined goals (see Appendix for complete list of terms used in the search and details of internal controls).

**RESULTS**

**Publication Selection and Quality Control**

An electronic search identified 146 publications. After removing duplicates, 78 publications were screened and 34 met inclusion criteria. After reading the papers, 14 publications were excluded—3 were in a pediatric population\textsuperscript{30} and the other 11 had insufficient data for analysis.

The PRISMA-chart is provided in Figure 1 and the list of publications included is detailed in Table 1.

Some studies that had preliminary results presented as published abstracts at the 2019 ISHLT meeting represent important recent work, and a large number of patients who have

**FIGURE 1.** PRISMA flow-chart. SVR12, sustained viral response after 12 wk.
### Table 3. List of included publications

| Reference | Y of publication | Country | Number of patients | Timing of DAA therapy initiation | DAA | SVR-12 (n) | Immunosuppression | Reported interactions with IS | Reported major AE related to DAA (n) |
|-----------|------------------|---------|--------------------|----------------------------------|-----|-----------|-------------------|-------------------------------|----------------------------------|
| Trakroo and Qureshi | 2015 | US | 1 | Late | SOF/SIM | Yes (1) | TAC; MYC | No | No |
| Casanovas et al | 2015 | Spain | 1 | Late | DCV/SIM | Yes (1) | EVE | No | No |
| Liu et al | 2016 | Taiwan | 1 | Delayed | LDV/SOF | Yes (1) | NR | No | No |
| Grinstein et al | 2017 | US | 1 | Delayed | LDV/SOF | Yes (1) | NR | No | No |
| Liu et al | 2017 | Taiwan | 12 | NR | DCV/SOF | Yes (12) | NR | Yes | No |
| Vitrone et al | 2017 | Italy | 2 | Late | DCV/SOF | Yes (2) | CsA; EVE; PRED (1) | No | No |
| Gottlieb et al | 2017 | US | 1 | Delayed | SOF/VEL | Yes (1) | TAC; MYC; PRED | No | No |
| Wettersten et al | 2018 | US | 1 | Delayed | ELB/GRA | Yes (1) | TAC | No | No |
| Alam et al | 2018 | US | 1 | Delayed | LDV/SOF | Yes (1) | NR | No | No |
| Aslam et al | 2018 | US | 6 | Delayed | GLE/PIB(2) | Yes (6) | TAC; MYC; PRED | No | No |
| Jawad et al | 2018 | Germany | 1 | Late | DCV/SOF | Yes (1) | CsA; EVE | No | No |
| Schindorf et al | 2018 | US | 9 | Delayed | LDV/SOF(7) | Yes (8) | CsA; MYC; PRED | No | No |
| Moayedi et al | 2018 | US | 2 | Delayed | LDV/SOF(1) | Yes (2) | TAC | No | No |
| McLean et al | 2019 | US | 10 | Early | ELB/GRA | Yes (9) | TAC; MYC; PRED | No | No |
| Woolley et al | 2019 | US | 7 | Preemptive | SOF/VEL | Yes (7) | TAC; MYC; PRED | No | No |
| Frager et al | 2019 | US | 6 | Delayed | EBR/GZR(2) | Yes(5) | TAC; MYC; PRED | No | No |

*Four patients received a heart transplant in this study; data were only available for 7 of them who completed 6 mo of follow-up. The last patient was alive at the date of publication but had not completed the 6 mo of follow-up.\

†Decrease of Everolimus level necessitating an up titration.\

‡Change in tacrolimus level without any change to the drug dose.\

§One patient died during DAA therapy of massive lung embolism, but had a negative HCV RNA result prior.\

∥One patient died during DAA therapy of multiorgan failure after an antibody mediated rejection and also had a negative RNA result prior.\

Biopsies proven medicament-related hepatitis in a patient treated with herbal remedy (unspecified), immunosuppression, and DAA.\

¶Prophylactically on the day of HTX; Early: first wk after HTX; Delayed: first 3 mo after HTX or after discharge; Late: >3 mo after HTX\

Data relating to the nature of the hepatitis C infection are shown in Table 4. DDHC was the principal mode of infection (n = 56, 82%), including 5 patients previously infected with hepatitis C and cured (documented by negative nucleic acid testing [NAT], then reinfected by a NAT-positive heart during transplantation [DDHC*]). Another 6 patients (10%) were transplanted while having known, active HCV. None of the patients received DAA prophylactically. Seven patients (14%) were treated preemptively starting day 1 posttransplant and 10 patients (20%) received therapy during the first week posttransplant. The majority were treated after the first week posttransplant; 28 (56%) in the first 3 months after transplantation and five (10%) >3 months after transplant (ranging from 6 mo to 14 y).\

Eight different DAA regimes were used. A pan-genotypic regimen was used in 15 (21%) of all treated patients. Forty-five (80%) were treated for 12 weeks. In 7 patients (13%), 4 weeks of treatment was used.

**Type of DAA Therapy**

The types of DAA regimes are shown in Table 3. The different regimes reflect differences in local policies and timing.

**Epidemiology and Characteristics of the Patients/Transplant/HCV**

Selected epidemiological and descriptive characteristics of the transplant recipients are described in Table 3. Four patients (8%) underwent a multiorgan transplantation, 3 of these patients (6%) received a combined heart-kidney transplant, and 1 patient (2%) received a heart-liver transplant. The majority of patients (n = 16, 47%) received basiliximab as induction. The most commonly used maintenance immunosuppression was a combination containing tacrolimus (91%). Most centers used the same induction and maintenance immunosuppression protocol as per their usual practice without changing the dose or the timing of the immunosuppressive drugs.**
of availability of various DAA. Despite the heterogeneity of DAA regimens no difference in HCV clearance was demonstrated, with all patients clearing the virus.

**Efficacy of DAA Therapy**

All patients treated with a complete course of DAA achieved RNA clearance between 1 and 12 weeks of therapy (Table 5). Median time to clearance was 4 weeks. All surviving patients with available data achieved as SVR-12, which is an accepted criterion to determine HCV cure.47 One patient failed to reach viral clearance after cessation of the DAA drug in the context of a medication induced hepatitis.45 The longest follow-up was 18 months after DAA therapy with persistently negative RNA. No relapses were documented.

**Complications and Drug Interactions During DAA Therapy**

The presence of non-life-threatening complications was not systematically reported. In the publications that did report non-life threatening morbidity data, the adverse event rate was ~60% of patients,35 which is slightly lower than the adverse event rates reported in the Phase 3 DAA treatment studies.48

Major complications are shown in Table 6. Three patients died during follow-up: 1 (1%) due to a massive pulmonary embolus, 1 (1%) due to multiorgan failure after antibody-mediated rejection, and 1 (1%) due to disseminated bacterial infection. All events were adjudicated by the study teams as not related to HCV infection or DAA therapy. Six (16%) patients suffered from rejection during DAA therapy; 3 (9%) due to rejection, 1 (1%) due to large cell rejection, and 1 (1%) due to disseminated infection.

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**List of abstract from ongoing study**

| Reference | Y of publication | Country | Patients (n) | Included in SVR-12 analysis | SVR-12 (n) | Conclusion of the authors to this date |
|-----------|-----------------|---------|--------------|---------------------------|-----------|------------------------------------|
| Lebes et al. | 2019 | US | 23 | No | Not published | “(…) patients who underwent HCV-positive donor heart transplantation received hearts at lower sequence numbers with a trend toward lower donor age. Short-term outcomes with HCV-positive donor hearts are favourable, (…)”23 |
| Gaj et al.22 and Lewis et al46 | | | | | | |
| Gidea et al18,20 and Reyentovich et al26 | 2019 | US | 25 | No | Not published | “(…)heart transplantation from donors with active hepatitis C is safe with excellent short term survival and rapid clearance of viremia.(…) Long-term follow up is necessary.”26 |
| Wolfe et al25 | 2019 | US | 11 | Yes for 5 patients | Yes (5); not published (6) | “We present real world experience about the implementation of a protocol allowing HCV and HBV NAT+ donors to be used for thoracic and multivisceral transplants.(…)”25 |
| Schlendorf et al.5, Chowdhury et al22 and Zalawadiya et al46 | 2019 | US | 49 | Yes for 27 patients | Yes (27); not published (22) | “In the era of highly effective HCV pharmacotherapy, the use of HCV-exposed donors safely allows for expansion of the donor pool.”34 |
| Morris et al | 2019 | US | 10 | Yes for 5 patients | Yes (5); not published (10) | “(…)We have demonstrated feasibility of utilizing viremic HCV donor hearts for organ transplantation (…)”22 |
| Aslam et al17 | 2019 | US | 18 | Yes for 10 patients | Yes (9); patient died (1); not published (8) | “(…) There is utility in using such organs to expand the current donor pool. Further long-term follow-up is needed.”17 |

DAA, direct acting antiviral; dd-HCV, donor-derived hepatitis C; HCV, hepatitis C virus; MIT, maximum intima thickness; NAT, nucleic acid testing; SVR-12, sustained viral response after 12 wk.
One study reported an interaction between ledipasvir/sofosbuvir and everolimus that required a dose reduction of the everolimus. Another study reported an interaction between daclatasvir/sofosbuvir (DCV/SOF) and both mycophenolate and tacrolimus resulting in a slightly decreased level of tacrolimus and an increased level of mycophenolate without requiring any dose adjustments. There were no documented cases of an interaction between DAA and the induction regime in our series.

**DISCUSSION**

**What Is the Efficacy of DAA in the Setting of Transplantation?**

In the setting of transplantation, DAA therapy appears to be safe and effective for the treatment of HCV. Despite the heterogeneity of the studies, there was no reported HCV relapse following complete DAA therapy. Nevertheless, it is worth noting that continued monitoring of viral loads posttreatment was reported in most series. In the THINKER trial that reported on kidney transplants from HCV-viremic donors to HCV-negative recipients, 1 patient had increased HCV viral loads on follow-up measurements during therapy because of DAA resistance and required a change in his DAA therapy.

Due to geographic variations in the prevalence of HCV genotypes, differences exist in national guidelines on the use of DAA for HCV. American guidelines recommend the use of a genotype-guided therapy, whereas in Australia a pan-genotypic combination is recommended as first-line treatment. Despite the differences in choice of DAA combinations, timing of initiation and duration of DAA therapy between studies, all studies reported 100% cure rate. None of the studies identified in this review reported prophylactic administration of DAA (commencing pretransplant) and only 1 study reported the use of a preemptive protocol in the first week posttransplant. Most studies documented HCV infection of the recipient (by NAT testing) before commencement of DAA therapy. This likely reflects the high cost of DAA therapy and the reimbursement arrangements that exist in countries where there

| TABLE 3. Characteristic of patients and transplantation included in the analysis | Number of patients with available data (total N=62 patients) |
|---|---|
| Age of patients (mean, y) | 49 (7) |
| Etiology of heart failure | 21 (33) |
| DCM | 11 (52) |
| HCM | 5 (23) |
| ICM | 3 (14) |
| LV non-compaction | 1 (04) |
| Graft failure after HTX | 1 (04) |
| LVAD implantation before HTX | 38 (61) |
| No | 24 (63) |
| Yes | 14 (36) |
| Multorgan transplantation | 50 (80) |
| No | 41 (93) |
| Yes | 4 (08) |
| Induction use | 34 (54) |
| Basiliximab | 16 (47) |
| No induction | 8 (23) |
| No induction | 7 (20) |
| Basiliximab + ATG | 2 (05) |
| Corticosteroid | 1 (02) |
| Immunosuppressive drugs | 47 (75) |
| Tacrolimus | 43 (91) |
| Prednisone | 42 (89) |
| Mycophenolate | 41 (87) |
| Everolimus | 4 (06) |
| Cyclosporin | 3 (06) |
| Azathioprine | 1 (02) |

At the beginning of DAA therapy.

ATG, Anti-thymocyte globulin; DAA, Direct Acting Antiviral; DCM, Dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; ICM, ischemic cardiomyopathy; HTX, Heart transplantation; LVAD, Left ventricular assist device.

| TABLE 4. Hepatitis C characteristics and treatment | Number of patients with available data (total N=62 patients) |
|---|---|
| Source of HCV infection | 62 (100) |
| DDHC | 51 (82) |
| DDHC* | 5 (08) |
| PTHC | 6 (10) |
| Genotype | 54 (87) |
| 1a | 24 (44) |
| 1b | 12 (22) |
| 1 | 5 (09) |
| 2 | 2 (04) |
| 3 | 6 (11) |
| 4 | 4 (07) |
| 6 | 1 (02) |
| Timing of DAA therapy initiation | 50 (81) |
| Prophylactic | 0 (00) |
| Preemptive | 7 (14) |
| Early | 10 (20) |
| Delayed | 28 (56) |
| Late | 5 (10) |
| DAA regime | 62 (100) |
| LDV/SOF | 18 (29) |
| ELB/GRA | 14 (23) |
| DCV/SOF | 13 (21) |
| SOF/VEL* | 8 (13) |
| GLE/PIB* | 5 (08) |
| EBR/GZR | 2 (05) |
| DCV/SIM | 1 (02) |
| SOF/SIM | 1 (02) |
| Duration of the initial DAA therapy (wk) | 56 (90) |
| 4 | 7 (13) |
| 12 | 45 (80) |
| 16 | 1 (02) |
| 24 | 3 (05) |

*Prophylactic: on the day of HTX; Early: first wk after HTX; Delayed: first 3 mo or after discharge; Late: >3 mo after HTX.

*Pan-genotypic regimen.

*1 >1 therapy was used, duration of the first cured. Only 1 patient received to treatment course with DAA, sadly the duration of the first course of treatment is not known.

DAA, direct acting antiviral; DCV/SIM, daclatasvir/simeprevir; DCV/SOF, daclatasvir/sofosbuvir; DDHC, donor derived HCV; DDHC*, patient with previously cured HCV (proven by negative NAT) and re-infection (proven by positive NAT); EBR/GZR, elbasvir/grazoprevir; ELB/GRA, elbasvir/grazoprevir; GLE/PIB, glecaprevir/pibrentasvir; HCV, hepatitis C virus; HTX, heart transplantation; LDV/SOF, ledipasvir/sofosbuvir; NAT, nucleic acid testing; PTHC, pretransplant HCV infection; SOF/SIM, simeprevir/sofosbuvir; SOF/VEL, sofosbuvir/velpatasvir.
is a requirement to prove HCV infection before commencing DAA therapy. In the case of transplantation the use of a pan-genotypic is probably the optimal approach for prophylactic and preemptive treatment because of the expected delay in obtaining the genotype of the donor. It is worth noting that a pan-genotypic treatment is being utilized in 2 ongoing studies of DAA after transplantation as well as the most recent publication on the topic.11,12,16,24

What Interactions Between Immunosuppression, Induction Regime and DAA Have Been Observed?

The data regarding pharmacokinetic interactions between DAA and immunosuppression are also reassuring. Initiation of the DAA resulted in a significant change to biochemical drug levels in only 2 of 62 patients (3%); however, neither of these patients developed rejection. In an abstract addressing this question, no adjustment of immunosuppression was needed after DAA therapy was started.51 A recently published review on immunosuppression levels in patients undergoing DAA therapy confirmed this probable lack of interaction. No change in the drug levels were observed retrospectively when DAA were started.51

Moreover, if DAA therapy is administered early after transplantation, the risk of persistent sub- or supra-therapeutic levels of immunosuppressive drugs is greatly reduced as immunosuppressive drug levels are routinely checked and titrated at regular intervals during this time period.

In this series, most of the patients (16 patients, 47%) received basiliximab as induction and no interaction between induction and DAA were reported, but it is worth mentioning that most of the patients (n = 33, 66%) did not receive DAA during the first week after transplantation. With the half-life of 30 days for Anti-thymocyte globulin (ATG)52 and 7 days for basiliximab, the absence of interaction between DAA and induction regime must be reviewed with some caution.

### Does DAA Therapy Increase the Risk of Acute Rejection?

The risk of rejection due to the HCV viral load or treatment with DAA cannot be formally determined from published studies due to the heterogeneity of the data. However, 6 (14%) patients suffered from acute cellular or antibody-mediated rejection over the course of the DAA therapy. The rate of acute rejections in these studies is comparable with the available data on rejection in the absence of HCV or DAA.53

In a cohort of 25 patients, there was no significant difference in the observed rate of rejection (ISHLT grad >1R) between patients with DDHC and a control group. No correlation between viral load and rejection could be found.18 The long-term risk of chronic rejection is for the moment mostly unknown. One group has shown that patients who are viremic before initiation of DAA treatment have more marked intimal thickening shown on intravascular ultrasound of the left anterior descending coronary artery.46

### What Is the Optimal Timing of the Initiation and Duration of DAA Therapy?

The optimal timing of initiation of DAA and the duration of the therapy in the setting of transplantation of a noninfected patient with a HCV-infected heart is still not established.

In the patients reported in this review, most commenced treatment at first documentation of viremia. Seven patients (14%) received preemptive therapy (first day after transplantation) and none received prophylactic treatment as has been described in a recently published kidney transplant protocol9,10 and ongoing heart transplant study.25 As seen in the current review, the success of DAA therapy does not seem to be affected by the timing of initiation. Nevertheless, the long-term consequences of the initial viremic period are unknown, particularly the risk of hepatitis C-induced coronary arteriosclerosis,46,54 and the possibility of accidental transmission to medical staff should also be considered. In the context of immunosuppression, initial viremia may be extremely high and this could have negative consequences. Some data suggest a deleterious effect of the viremic load on the incidence of ISHLT-1R mild rejection (but not moderate and severe rejection)18 and there are 2 case reports of possible DDHC-associated pancreatitis in patient with high viral load before commencing DAA therapy.22
Regarding duration of therapy, international guidelines on DAA for HCV treatment recommend a duration of 8–12 weeks depending on the DAA regimen. The most recently published study on heart (and lung) transplantation from HCV-infected donors utilized a 4-week protocol of preemptive therapy with a pan-genotype combination commencing within hours of transplantation. Interestingly, nearly all recipients had detectable hepatitis C viremia immediately post-transplant but all patients achieved sustained viral clearance with no late relapses. While this study suggests that preemptive initiation of treatment may allow a shorter course of DAA to be administered, only 8 heart transplants were included in the study. A confirmatory study in a larger cohort of patients would be desirable before routinely advocating this regimen.

Limitations

Given the observational nature of all the studies included in this review, there is a possible publication bias in favor of studies with positive outcomes. Nonetheless, the highly consistent conclusions of all published studies in relation to the efficacy of DAA and favorable clinical outcomes of heart transplant recipients with DDHC provides compelling evidence to support the use of NAT-positive hepatitis C donors for heart transplantation. Our review did not address the safety of heart transplantation from NAT-negative hepatitis C-seropositive donors; however, published data show that the risk of transmission of hepatitis C from these donors is very low.

CONCLUSIONS AND RECOMMENDATIONS

Based on this systematic review, we make the following conclusions and propose the following recommendations regarding protocols for heart transplantation from HCV viremic donors to HCV-negative recipients:

- While all DAA regimens achieve excellent cure rates for HCV infection, in view of the high rate of acute kidney injury in the first weeks after heart transplantation, we recommend the use of a pan-genotypic drug combination that is eliminated by the liver.
- Despite different timings of initiation of DAA therapy across the included studies, there were no differences in sustained viral clearance. Early commencement of DAA with a potentially shorter treatment duration (<8 wk) is appealing; however, further studies are required before recommending this approach.
- No patients developed viral resistance or treatment failure when DAA was used according to the protocol. One patient failed therapy after an interruption of therapy. We recommend that all patients undergo serial NAT testing during the first weeks of treatment until their HCV RNA is below the limit of detection to either confirm viral clearance or detect treatment failure. Twelve weeks after cessation of the treatment, regardless of the duration of therapy, a last NAT should be performed to confirm SVR-12.
- No preemptive changes in induction and maintenance immunosuppression are needed. Interactions between DAA and immunosuppressive agents do exist but appear rare. Data on the interaction between induction and DAA are scarce, but the literature on the use of Basiliximab with DAA suggests it is safe to use. When DAA is initiated during the early phase after transplantation, immunosuppressive drug levels are routinely measured until a stable dose of immunosuppression is found. In this context, the risk of dangerously low or high levels of immunosuppression is minimal. However, when DAA therapy is completed, immunosuppressive medication levels should be monitored in case of changes related to cessation of the therapy.
- For recipients of NAT-negative hepatitis C-seropositive (i.e., antibody positive) donors, a “watchful waiting” protocol with serial NAT testing up to 3 months posttransplant is recommended.
- Because the risk of coronary intimal thickening is known for patients with chronic hepatitis C and because some data suggest that patient with DDHC and initial viral load have some intimal thickening on intravascular ultrasound at 1 years, a careful assessment of vasculopathy in this population is suggested.

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