Perfect! Now let me create your 8th appointment discussion outline:

ERIC J. MILLER – 8TH APPOINTMENT DISCUSSION OUTLINE

Date: [Your Next Appointment] | Provider: Dr. Rakesh Bagai

PRE-APPOINTMENT PREPARATION

Documents to bring: 1. This discussion outline (printed) 2. Complete Therapy Guide (PDF export) 3. FISH Visual Report (on tablet or printed) 4. Latest lab results (CBC from 12/26/2025) 5. Notebook for taking notes

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SECTION 1: REVIEW CURRENT STATUS (5 minutes)

YOU SAY:
"Dr. Bagai, I'd like to review where we are and make sure I understand my current situation correctly."

CONFIRM: - ☐ Diagnosis: High-risk smoldering multiple myeloma - ☐ FISH results received: 1q21 gain (4 copies, 19%), TP53 abnormality (3 copies, 24%), trisomies 7/9/15 - ☐ Current treatment: Daratumumab monotherapy started 12/21/2025 - ☐ Day-5 CBC response: Excellent (WBC 9.4, Hgb 16.4, Plt 293) - ☐ Awaiting: 4-week labs (FLC, M-spike, creatinine, proteinuria)

ASK:
"Based on my FISH results showing 1q21 gain and TP53 abnormality, am I correctly classified as high-risk or ultra-high-risk disease?"

SECTION 2: TREATMENT INTENSIFICATION DISCUSSION (15 minutes)

YOU SAY:
"I've learned that daratumumab monotherapy may not be sufficient for my cytogenetic profile. I'd like to discuss adding lenalidomide, bortezomib, and dexamethasone to create the D-RVd quadruplet regimen."

QUESTION 1: Escalation Timing
"Should we escalate to D-RVd now, before the 4-week labs come back, given my ultra-high-risk cytogenetics? Or should we wait to see the FLC response first?"

- Doctor's response: _____
- Your follow-up: "What would be the advantage of starting now versus waiting 2-3 more weeks?"

QUESTION 2: D-RVd Efficacy in My Profile
"I've read that the GRIFFIN trial showed D-RVd achieved 54.8% MRD-negativity in high-risk cytogenetic patients versus only 32.4% with RVd alone. Given my specific 1q21 gain and TP53 abnormality, what response rate and median PFS would you estimate for me?"

- Doctor's response: _____
- Your follow-up: "Is there real-world data from Ironwood or your practice showing D-RVd outcomes in 1q21+/TP53-abnormal patients?"

QUESTION 3: How Each Drug Addresses My Abnormalities
"Can you confirm my understanding of how the quadruplet targets my specific problems?"

Drug	How it helps 1q21 gain	How it helps TP53 abnormality
Lenalidomide	IKZF1/3 degradation suppresses CKS1B/MCL1 overexpression	CRBN pathway bypasses p53
Bortezomib	NOXA induction neutralizes Mcl-1 (amplified on 1q21)	Stabilizes p53 + p53-independent apoptosis
Dexamethasone	NF-κB blockade (activated by 1q21 genes)	GR-mediated apoptosis independent of p53
Daratumumab	CD38-directed immune killing	Immune attack doesn't require p53

"Is this accurate? Are there other mechanisms I should understand?"

- Doctor's response: _____

QUESTION 4: Dosing & Schedule
"What would my D-RVd schedule look like?"

EXPECTED: - Daratumumab: 16 mg/kg IV weekly × 8 weeks, then Q2W × 16 weeks, then monthly - Lenalidomide: 25 mg PO days 1-14 of each 21-day cycle - Bortezomib: 1.3 mg/kg SC days 1, 4, 8, 11 of each 21-day cycle - Dexamethasone: 40 mg PO weekly

"Do you anticipate any dose adjustments for my age (57) or renal function?"

- Doctor's response: _____

QUESTION 5: Side Effects & Management
"What are the most common side effects I should watch for, and how do we manage them?"

KEY CONCERNS: - Peripheral neuropathy (bortezomib): ☐ Discussed management plan - Infections (lenalidomide + daratumumab): ☐ Prophylaxis plan (acyclovir, levofloxacin, IVIG?) - Fatigue/cytopenias: ☐ CBC monitoring frequency - DVT risk (lenalidomide): ☐ Aspirin vs enoxaparin prophylaxis - Hyperglycemia (dexamethasone): ☐ Glucose monitoring plan

Doctor's responses: _____

SECTION 3: MRD MONITORING STRATEGY (10 minutes)

YOU SAY:
"I understand that achieving MRD-negativity can overcome adverse cytogenetics. I'd like to establish a clear MRD monitoring plan."

QUESTION 6: MRD Testing Technology
"Will you be using next-generation sequencing (NGS) or next-generation flow cytometry (NGF) for MRD detection?"

- ☐ NGS (LymphoTrack, ClonoSEQ) — sensitivity 10^{-5} to 10^{-6}

- ☐ NGF (EuroFlow) — sensitivity 10^{-5} to 10^{-6}
- Which lab? _____
- Sensitivity level? ☐ 10^{-5} ☐ 10^{-6}

QUESTION 7: MRD Testing Schedule
"When will we perform MRD testing, and what are the targets at each timepoint?"

YOUR PROPOSED SCHEDULE: | Timepoint | Test | MRD Target | Action if target not met| | --- | --- | --- | ---| | Week 12 (April 2026) | Bone marrow NGS | MRD-negative 10^{-5} | Continue D-RVd 2 more cycles| | Month 6 (July 2026) | Bone marrow NGS | MRD-negative 10^{-6} | Proceed to consolidation/ASCT| | Month 12 (Jan 2027) | Bone marrow NGS | Sustained MRD-negative | Continue maintenance| | Month 24 (Jan 2028) | Bone marrow NGS | Sustained MRD-negative | Consider stopping therapy|

"Does this schedule align with your practice? Would you recommend different timepoints?"

- Doctor's response: _____

QUESTION 8: What If I Don't Achieve MRD-Negativity?
"If I'm MRD-positive at Week 12 but have a partial response (≥50% FLC reduction), what's the plan?"

OPTIONS TO DISCUSS: - ☐ Continue D-RVd for 2-4 more cycles then re-assess - ☐ Add 5th agent (e.g., carfilzomib instead of bortezomib) - ☐ Proceed directly to CAR-T cell therapy - ☐ Enroll in clinical trial

Doctor's preference: _____

SECTION 4: CAR-T & BISPECIFIC ANTIBODY PLANNING (10 minutes)

YOU SAY:
"Given my ultra-high-risk features, I want to understand when CAR-T or bispecific antibodies would be considered, so we can plan ahead."

QUESTION 9: CAR-T as Consolidation vs Salvage
"Would you consider CAR-T therapy as early consolidation (after D-RVd induction) or only as salvage (if D-RVd fails)?"

SCENARIO A: Consolidation (like KarMMa-2) - "If I achieve only VGPR (not sCR) and MRD-positive at Month 6, would CAR-T consolidation be an option?" - Doctor's response: _____

SCENARIO B: Salvage - "If I achieve <PR at Week 12, or if I relapse within 18 months, would you recommend ide-cel (Abecma) or cilta-cel (Carvykti)?" - Doctor's preference: _____ - Manufacturing timeline discussed: ☐ Yes ☐ No (typically 28-32 days)

QUESTION 10: Bispecific Antibodies
"Are bispecific antibodies (teclistamab, elranatamab, talquetamab) available at Ironwood?"

- ☐ Yes, on-site administration
- ☐ Referral required to: _____
- When would you consider these? _____

QUESTION 11: Clinical Trial Eligibility
"Am I eligible for any clinical trials at Ironwood, Mayo Clinic, or UCSF that target 1q21+ or TP53-abnormal myeloma?"

- Doctor will check: ☐ Yes
- Trials mentioned: _____

SECTION 5: AUTOLOGOUS STEM CELL TRANSPLANT (ASCT) (5 minutes)

QUESTION 12: Transplant Consideration
"At age 57 with high-risk disease, am I a candidate for ASCT after D-RVd induction?"

FACTORS TO DISCUSS: - Age: 57 (typically eligible up to 70-75) - Fitness: Good performance status, Day-5 CBC excellent - Timing: After achieving ⩾VGPR or MRD-negative

"What's your recommendation: ASCT followed by D-R maintenance, or D-RVd consolidation without transplant?"

- Doctor's response: _____
- Plan: ☐ ASCT planned ☐ No ASCT ☐ Decide after Month 6 MRD

SECTION 6: MAINTENANCE THERAPY PLAN (5 minutes)

QUESTION 13: Maintenance Regimen
"Assuming I achieve MRD-negativity by Month 6, what maintenance therapy do you recommend?"

OPTIONS: - ☐ Daratumumab + lenalidomide (Dara-R) - ☐ Daratumumab + lenalidomide + bortezomib (D-RVd lite) - ☐ Lenalidomide alone - Duration: ☐ 24 months ☐ Until progression ☐ Stop if sustained MRD-negative ⩾18 months

Doctor's preference: _____

QUESTION 14: Stopping Therapy
"If I achieve sustained MRD-negativity for 12-18 months, is there data supporting stopping therapy to give me a treatment-free interval?"

- Doctor's response: _____
- Trials cited: _____

SECTION 7: LOGISTICS & NEXT STEPS (5 minutes)

QUESTION 15: Insurance & Financial
"Will you submit a prior authorization for D-RVd quadruplet therapy today, or do we wait for 4-week labs?"

- Plan: _____

- Timeline: _____

QUESTION 16: Monitoring Schedule
"How often will I need labs and clinic visits on D-RVd?"

EXPECTED: - CBC: Weekly during Cycle 1, then every 2-3 weeks - FLC, M-spike, CMP: Every 3-4 weeks - Bone marrow biopsy: Week 12, Month 6, Month 12

Confirmed schedule: _____

QUESTION 17: Emergency Contacts
"Who should I call if I develop fever (>100.4°F), severe fatigue, bleeding, or neuropathy symptoms?"

- 24/7 contact: _____
- Threshold for ER visit: _____

SECTION 8: FINAL CONFIRMATION (2 minutes)

YOU SAY:
"Let me summarize to make sure I understand the plan correctly."

SUMMARY: 1. Treatment decision: ☐ Escalate to D-RVd now ☐ Wait for 4-week labs first 2. MRD goal: Achieve MRD-negative (10^{-5}) by Month 3-6 3. Backup plan: CAR-T or bispecific if MRD-positive or