Combined Protocol of DCA with Poly-MVA (LAMC):

In 2009 as part of a "non-responder" arm of an NIH funded trial we (7) surmised a potential synergy of LAMC and DCA. A cell line study (1,8) showed apoptotic cell synergy in GBM cells. Additionally chemically the two agents have a potential for physiologic mutual benefit. The potential physiological benefit is that typical DCA use requires cell protective support during treatment and LAMC has been shown to be neuroprotective and supportive to the mitochondrial complex. (2,3,4,5) The author had used DCA with supportive nutrients prior to this and abandoned its use due to a high side effect profile.

Protocol as developed originally in the NIH funded trial in conjunction with Anderson Medical Specialty Associates / Advanced Medical Therapies can be found in the archived resources. (7,8,9) The evolved protocol in current use is explained below.

Protocol Overview:

1. Dietary Intervention
2. Use of supplemental retinol
3. Use of either oral or intravenous PolyMVA and DCA
4. Addition of hyperbaric oxygen therapy (HBOT) if available

1. Dietary Intervention:

- Patients are on a ketogenic or (at least) low carbohydrate diet
- Oral ketone supplements starting at 2.5 grams BID and increasing to 5 grams BID as tolerated.

2. Retinol Rx:

Patients are given Vitamin A: 25,000 IU Retinol in a fat soluble (not carotenoid) form PO QD

3. Administration of PolyMVA and DCA either orally or intravenously as outlined below:

All administration dosing and guidelines are found below.

4. Use of concurrent HBOT:

We begin at an 1.3 to 1.5 ATA trial, bottom time 30-45 minutes with O2 by mask. Dive may be increased to 2.0 ATA X 60 minutes (we have not found this necessary). At higher ATA air breaks may be required up to 5 minute break per 15 minutes of dive time.

Specific Protocol Information:

A. IV Protocol:

First IV: Poly-MVA (LAMC) diluted as noted below in Normal Saline or D5W and administered over 75 to 90 minutes.

- Always administer the LAMC IV first
- No other additives are mixed in the LAMC IV
- For dosing in children use Clark's rule: **Appendix A**

Second IV: DCA dosed by body weight in normal saline as listed below and administered over 90-120 minutes minimum.

B. Oral Protocol:

- Oral Poly-MVA: Up to 40 mL (8 teaspoons) daily (divided doses) BID
  - As an example a patient at 40 mL is given 20 mL PO BID
  - This may be administered at the same time as the DCA
- Oral DCA: 20 mg/kg PO (divided doses) BID
  - As an example if the total daily dose is 20 mg/kg; give 10 mg/kg PO BID

Intervention Schedule:

Dose schedule is four to five days weekly if tolerated at a rotation of four to five days on medication and two to three days off medication per week.

If detoxification symptoms such as headache, itching, non-anaphylactic skin erythema or others occur a three day per week alternating schedule of three days on protocol and four days off protocol may be attempted. As an example: Monday - Wednesday – Friday on protocol and the balance of the days off.

Monitoring for reactions to therapy:

Detoxification symptoms of DCA as typically mediated by glutathione S-transferase zeta (GSTz) are generally responsive to increased thiol support with IV glutathione, oral Alpha Lipoic Acid or N-Acetyl Cysteine, but are much rarer in this combined therapy as the LAMC in the authors experience has a greater protective effect.

Patient reactions can include fatigue, headache, temporary cognitive effect ("brain fog"), lethargy, body aches and other symptoms associated with glutathione detoxification effect.

If these symptoms occur consider lowering the dose of both agents, adding a 250 – 500 mL normal saline (NS) IV prior to the PolyMVA, spreading the IV treatments out over a longer period or all of the above. Clinical reassessment is critical in attenuating these events.

Assessment of therapy:

Most trial periods for the above therapy are eight to twelve weeks, or until the next interval imaging or other assessment is reached. In the authors experience if either regression of disease or stable disease is reached then a clinical decision must be made as to continuing at the above aggressive schedule or decreasing the number of days treated weekly. This typically is dependent on the aggressiveness and intensity of the oncologic process being treated.

A typical "withdrawal trial" in a positive responder (if less therapy is clinically indicated) is to decrease to 3 days on medication and four off per week for an interval of eight to twelve weeks before re-assessment. Any disease progression during this time should be met with a return to the prior treatment schedule.

Specific IV body weight dosing as referred to in the above protocol outline:

FIRST IV ADMINISTERED: Poly-MVA [Note: dilute 1 – 15 mL in 250 NS / 16 – 40 mL in 500 NS]

Body Weight	Test Dose	Second IV	Third IV	Max dose:
50 kg	**5 mL**	**15 mL**	**20 mL**	**40 mL**
60 kg	**5 mL**	**15 mL**	**20 mL**	**40 mL**
70 kg	**5 mL**	**15 mL**	**30 mL**	**40 mL**
80 kg	**10 mL**	**20 mL**	**30 mL**	**40 mL**
90 kg	**10 mL**	**20 mL**	**30 mL**	**40 mL**
100 kg	**10 mL**	**20 mL**	**30 mL**	**40 mL**
> 100 kg	**10 mL**	**20 mL**	**30 mL**	**40 mL**

LAMC ACTIVE INGREDIENT		MG PER ML	5ml	10ml	20ml	40ml
ALA/Thiamin mg ≈		8/9mg	35/40mg	70/80mg	140/160g	280/320mg
Lipoic Acid Mineral Complex ≈		**21mg**	**105mg**	**210mg**	**420mg**	**840mg**
Co-Facgors						
B2 Riboflavin		.2mg				
B12 as cobalamin		.2mg				
Molybdenum						
Rhodium						
Ruthenium						
Formyl Methionine						
N-AcetylCystein						
Total Co-Factors ≈		**0.5mg**	**1.25mg**	**2.5mg**	**5.0mg**	**10mg**
Sodium (mg) ≈		3mg	15mg	30mg	60mg	120mg

SECOND IV ADMINISTERED: DCA

Body Weight	Test Dose	30 mg/kg	50 mg/kg	65 mg/kg	80 mg/kg
50 kg	**500 mg**	**1500 mg**	**2500 mg**	**3250 mg**	**4000 mg**
60 kg	**600 mg**	**1800 mg**	**3000 mg**	**3900 mg**	**4800 mg**
70 kg	**700 mg**	**2100 mg**	**3500 mg**	**4550 mg**	**5600 mg**
80 kg	**800 mg**	**2400 mg**	**4000 mg**	**5200 mg**	**6400 mg**
90 kg	**900 mg**	**2700 mg**	**4500 mg**	**5850 mg**	**7200 mg**
100 kg and over	**1000 mg**	**3000 mg**	**5000 mg**	**6500 mg**	**8000 mg**

Patients taking Metformin:

While synergy has been shown in vivo between DCA and Metformin (10,11) the author has observed aggravation of the above mentioned DCA side effects in some, but not all, patients taking metformin. If this is observed the recommendation is to decrease the metformin dose by ½ on DCA administration days in diabetics and to hold the metformin in non-diabetics on DCA treatment days. The plasma half life is short (+/- 6 hours) so this decrease or discontinuance of the metformin has negligible blood sugar effect in most patients.

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Appendix A:

Clark's Rule is a medical term referring to a procedure used to calculate the amount of medicine to give to a child aged 2-17. The procedure is to take the child's weight in pounds, divide by 150lbs, and multiply the fractional result by the adult dose to find the equivalent child dosage.

Pediatric dose = [child's weight (lb) / 150 (lb)] x Adult dose

For example: If an adult dose of medication calls for 30mg and the child weighs 30lbs. Divide the weight by 150 (30/150) to get 1/5. Multiply 1/5 times 30mg to get 6mg. (Or convert the fraction to a decimal and multiply – 0.20 in this case). **Common IV example:** Adult goal dose is 40 mL Poly-MVA

Child weighs 25 pounds: [25 lb / 150 lb] x 40 mL 1/6 x 40 mL [convert to a decimal]
0.167 x 40 mL = 6.7 (7) mL dose