POLY-MVA (LAMC) IN COMBINATION WITH OTHER IV THERAPIES

Poly-MVA (LAMC) is an <u>incredible synergist</u> in many IV/oral therapy sequences. Below are recommendations for infusion in proximity or separately from other particular therapies based on cellular actions of LAMC as well as the other therapies below. The purpose of these recommendations is to make maximal use of the potential for therapeutic synergy with a unique redox molecule LAMC.

Compiled by Dr. Paul Anderson

Infuse separately:

Separate LAMC from these therapies by 4-6 hours (ideally LAMC infusion first then these IV's later in the day or any time on the following day.):

- Artesunate with High Dose IV Ascorbate
- High Dose IV Ascorbate
- Ozone
- Hydrogen Peroxide
- Mistletoe (IV) products [SQ Mistletoe does not apply]

The therapeutic goal is to have the LAMC in the cells and working before these other therapies are circulating in the blood.

Infuse in proximity:

Infuse LAMC in sequence / at the same IV sitting with:

- Curcumin (low or high dose, give LAMC first)
- Artesunate with low dose IVC (give LAMC first) Example ART-LDIVC as used in autoimmunity.
- Water soluble vitamin mineral and / or amino acid formulas **
- Glutathione **
- Phosphatidylcholine **

** LAMC may be given before these, ideally after any of these therapies.

Lipoic Acid Mineral Complex In Fatigue, Mitochondrial & Neuro-inflammatory Disorders

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At our clinic, Anderson Medical Specialty Associates in Seattle Washington, we have been working with LAMC in various clinical settings:

- 1. Oncology treatment
- 2. Oncology Quality of Life

- 3. Chronic illness treatment
- 4. Chronic illness Quality of life

Our investigation of the LAMC "PolyMVA" in the areas of chronic neuro-degenerative illnesses, Chronic Fatigue/ Fibromyalgia and mitochondrial illness has led to a potentially unique and novel role in the treatment of those conditions.

As part of a multi agent therapy our experience has been that we see better outcomes when using IV PolyMVA over standard IV ALA.

Additionally our use of oral PolyMVA as maintenance has shown positive results for quality of life in preliminary feedback.

Lipoic Acid Mineral Complex /PolyMVA: Mechanism of Action

The Lipoic Acid Mineral Complex (LAMC):

Known as the proprietary formula "Poly MVA" in North America, LAMC has shown to be helpful in cell repair, mitochondrial repair and radioprotection [1-4]. The author has found that low IV doses (5-40 mL) combined with low oral doses (5-40 mL BID) improve energy and other quality of life measures in FMS/CFS patients. Like ALA, LAMC does take time to work so most patients are advised that either therapy (like all others) may need to be continued for a number of months for a positive effect to be noted.

LAMC (PolyMVA) IV **Start with a 5ml TEST DOSE AND RAMP UP AS TOLERATED

- > We have used IV PolyMVA in the setting of chronic disease and mitochondrial damage and dysfunction.
- Doses in the fatigue mitochondrial injured neurodegenerative population need to be lower and ramped up more slowly than in the oncology patient.
- > IV dose is mixed in 100 250 mL Normal Saline or D5W and administered over 20 to 600 minutes.
- > For Children use Clark's rule
- Ramp up to 20-40 mL
- > Give in series (as a separate bag) with other nutrients, No other additives are mixed
- Dose is once to three times weekly

^{1.} Menon, A., and Nair, C.K.K. (2011) Poly MVA – a dietary supplement containing alpha-Lipoic Acid Mineral Complex, enhances cellular DNA repair. Int. J. Low Radiation, in print. 2. Ramachandran, L., Krishnan, C.V., Nair, C.K.K. (2010) Radioprotection by a-Lipoic Acid Mineral Complex formulation, (POLY-MVA) in mice, Cancer Biotherapy and Radiopharmaceuticals, Vol. 25, No.4, 395-399. 3. Menon, A., Krishnan, C.V., Nair, C.K.K. (2009) Protection from gamma-radiation insult to antioxidant defense and cellular DNA by POLY-MVA, a dietary supplement containing palladium lipoic acid formulation. Int. J. Low Radiation, Vol. 6, No.3, 248-262.4. 4. Menon, A., Krishnan, C.V., Nair, C.K.K. (2008) Antioxidant and radio protective activity of POLYMVA against radiation induced damages, Amala Cancer Bulletin, Vol 28, 167-173

PolyMVA / LAMC IV Multi Agent Therapy

The following is the basic format for the protocol AMSA has used with the chronically ill: Typical series is (1) Vitamin-Mineral Bag, (2) Glutathion and then (3) IV LAMC. We typically use for 8 weeks and then reassess.

First IV: IV Vit/Mineral formula cofactors for mitochondrial and glutathione function Second IV: Glutathione Third IV: Phosphatidylcholine Fourth IV: PolyMVA Doses for PolyMVA as above: Doses for the other agents are as given in standard training courses.

PolyMVA / LAMC IV Multi Agent Therapy

Preliminary Outcomes

- When given to patients with chronic illness the multi-agent IV therapy above has been well tolerated and shown positive symptomatic and quality of life changes.
- In two particular patients where the multi-agent therapy above had been given with ALA in place of the PolyMVA the patients reported better results symptomatically when the PolyMVA was returned to the protocol.

LAMC (PolyMVA) Oral

- > We have used oral PolyMVA in chronic disease and mitochondrial damage and dysfunction.
- > Oral doses can be 5 to 40mL (1-8 teaspoon) BID
- > These are used as support between IV treatments or stand-alone.
- > Generally this is dosed four to five days per week for up to 8-12 weeks

Summary

- Our clinical experience in oncology patients led us to begin to try to use PolyMVA in the chronically population. Our experience in hundreds of administrations of PolyMVA to patients showed safety in both IV and Oral use.
- Additionally we had the background of PolyMVA providing improved quality of life in the oncology population.
- When we added PolyMVA to our multi-agent IV and Oral therapy for chronically ill patients we also have noticed improved response in symptoms and Quality of Life.
- We believe as we continue to track data on patient outcomes we will see improved parameters of symptom and potentially disease mitigation.

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 1.5 ATA X 60 minutes. At higher ATA air breaks may be required up to 5 minute break per 15 minutes of dive time. With the full protocol one to three HBOT dives per week are optimal.

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

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COMBINED METABOLIC ONCOLOGY PROTOCOL: ANDERSON

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
 - \circ $\,$ As an example a patient at 40 mL is given 20 mL PO BID $\,$
 - o 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 <u>headache</u>, itching, non-anaphylactic skin erythema or others occur a <u>three day per week alternating schedule</u> 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:

<u>Detoxification symptoms of DCA</u> 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 <u>include fatigue</u>, <u>headache</u>, <u>temporary cognitive effect ("brain fog"</u>), <u>lethargy</u>, <u>body</u> <u>aches and other symptoms</u> 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 reassessment. Any disease progression during this time should be met with a return to the prior treatment schedule.

COMBINED METABOLIC ONCOLOGY PROTOCOL: ANDERSON

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 \approx	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 \approx	0.5mg	1.25mg	2.5mg	5.0mg	10mg
Sodium (mg) \approx	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	1000 mg	3000 mg	5000 mg	6500 mg	8000 mg
over	1000 mg	5000 mg	5000 mg	0500 mg	8000 mg

COMBINED METABOLIC ONCOLOGY PROTOCOL: ANDERSON

Patients taking Metformin:

While synergy has been shown in vivo between DCA and Metformin (10,11)/ Poly and Metformin 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 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

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Lipoic Acid Mineral Complex Adjunctive Protocol Fatigue - Neurological - Cancer – Lyme - Palliative Care

Frequency Options and dosage will vary from 5-60cc's:

a. Targeted Protocol 5 days per week for 4 consecutive weeks and evaluate

b. Blended 2-3 days per week for 12 consecutive weeks and evaluate

c. Intermittently to coincide with or around other IV protocols or treatments

(e.g., Various types of integrative IV's, chemo or radio therapy used before and after)

Regimens can be repeated multiple times with combination and Press/Pulse protocols.

Improved outcomes when Oral Poly is used before, during & after the IV protocols.

The patient will then be doing both the IV LAMC and oral Poly simultaneously. The advanced oral dose is 8-12 tsp per day (2-3 tsp four times per day) or 1-4 tsp based on the minimum dose that is used on off days (NON- IV days), and 1-2 tsp am and pm on days they do receive the IV LAMC.

After the IV protocol is completed, maintain the patient on the maximum oral dose for at least 2-3 months or longer as needed. Then begin gradual oral taper as needed.

The minimum effective dose for continuing patients, depending on body weight is at least 1-4 tsp per day.

It appears synergistic with various protocols and other agents based on research, doctors' reports and observed clinical responses. Additional ALA is not needed or recommended when using LAMC.

Intra Muscular and Sub cutaneous injections

IM up to 3-5cc using deltoid, ventrogluteal injection or Posterior gluteal injection or Sub Q 1-3 cc

IV preparation and administration:

1. Generally start with 100-250cc normal saline. Initially add 5-15 cc of injectable LAMC.

Increase each infusion by 5-10 cc of IV LAMC until max of 40-60 cc or 0.6-0.9 cc per kg (based on a 70 kg patient). Continue at the max dose as tolerated for the remainder of the protocol.

- 2. Run the 100 cc infusions over 30-45 minutes.
- 3. 10-20cc 3 times for first week with oral dosage of 10-20 cc on all days.
- Dosage can increase to 30/60 cc of IV LAMC, increase to 250/500/1000 cc of saline. Run this over one hour or more.
- 5. 30-40cc 3 times for second week with oral dosage of 10-40cc
- 6. 40-60cc 3 times for third week with oral dosage of 20-40cc on days off and weekends.

Off IV LAMC days- Use O<u>ral</u> Poly-MVA between 5-40ml per day